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1. EFFECTS OF PROXIMAL VERSUS DISTAL ENTERECTOMY ON GASTRIC SECRETION
2. EFFECTS OF MASSIVE ENTERECTOMY AND AN ANTIPERISTALTIC SEGMENT ON  
GASTRIC SECRETION

by



ADRIAN HOBART

A THESIS

SUBMITTED TO THE FACULTY OF GRADUATE STUDIES

IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE

OF MASTER OF SCIENCE

DEPARTMENT OF SURGERY

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THE UNIVERSITY OF ALBERTA  
FACULTY OF GRADUATE STUDIES

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies for acceptance, a thesis entitled

1. Effects of Proximal Versus Distal Enterectomy on Gastric Secretion
2. Effects of Massive Enterectomy and an Antiperistaltic Segment on Gastric Secretion

submitted by Adrian Hobart, in partial fulfilment of the requirements for the degree of Master of Science (Surgery).





## ABSTRACT I

Massive enterectomy is followed by gastric hypersecretion. The mechanism for this phenomenon is not known, although evidence suggests that it may be hormonally mediated. The effects of proximal and distal enterectomy on Heidenhain Pouch secretion in dogs, and the effects of thoracic duct lymph diversion and thoracic duct lymph reinfusion on these enterectomized dogs were studied.

Baseline Heidenhain Pouch secretory studies were made under awake and anaesthetized, fed and fasting conditions, on twelve dogs. Six then had a 55% proximal enterectomy (Group A), and six a 55% distal enterectomy (Group B). In all dogs the stomach and duodenum were left intact. In the twenty-four hour collections, both groups showed a Heidenhain Pouch hypersecretion. In the eight hour studies, Group A dogs hyposecreted, while Group B maintained their hypersecretion. By contrast, when the diverted thoracic duct lymph was reinfused, the dogs of Group A hypersecreted, while the Heidenhain Pouch secretions of Group B remained unchanged.

Our findings have demonstrated an unsuspected difference in Heidenhain Pouch secretion between proximal and distal enterectomies. Our results have shown a distal resection to be more effective than a proximal one in producing gastric hypersecretion. The thoracic duct lymph diversionary studies offer evidence of a secretagogue; the





decreased Heidenhain Pouch secretion in Group A dogs suggests an ileal inhibitor to gastric secretion. Possible explanations, and clinical implications of these phenomena are discussed.





## ABSTRACT II

Death from cachexia within ninety days follows resection of 80% of the small intestine in the dog. In the present study, 90% of the small intestine was resected in six dogs, and the subsequent deterioration allowed to proceed for approximately half the expected survival time. At this time, an 8 cm. length of proximal jejunum was reversed to act as an antiperistaltic segment. Ninety days after this procedure, the dogs were alive and healthy; the steep fall in body weight that followed massive enterectomy had been arrested, and the mean body weight had stabilized at 75% of the control figure. Barium x-ray studies demonstrated a delay in gastric emptying time after insertion of the antiperistaltic segment. The control time of four and one-half hours rose to six hours after segmental reversal.

Although the therapeutic application of this experiment is clear, one of the undesirable sequelae of the operation was an increase in gastric secretion of up to 372% of the control value. The possible reasons for these findings are discussed.



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## TABLE OF CONTENTS

PART 1. EFFECTS OF PROXIMAL VERSUS DISTAL ENTERECTOMY  
ON GASTRIC SECRETION

	PAGE
REVIEW OF PHYSIOLOGICAL REGULATION OF GASTRIC SECRETION . . . . .	1
I. Vagal Mechanism . . . . .	2
II. Antral Mechanism . . . . .	6
III. Intestinal Mechanism . . . . .	10
IV. Miscellaneous . . . . .	17
Visceral . . . . .	17
Local Factors . . . . .	19
Work Challenge . . . . .	20
V. Conclusion . . . . .	21
METHODOLOGY . . . . .	32
I. General . . . . .	32
II. Experimental Plan . . . . .	32
III. Before Operation . . . . .	33
IV. Operation . . . . .	34
V. Heidenhain Pouch Construction . . . . .	34
VI. Proximal Enterectomy . . . . .	36
VII. Distal Enterectomy . . . . .	38
VIII. Thoracic Duct Cannulation . . . . .	38
IX. Postoperative Management . . . . .	40
X. Collection of Samples . . . . .	41



XI. Determination of Gastric Acidity, . . . . .	42
RESULTS . . . . .	45
I. First Stage . . . . .	45
Twenty-Four Hour Measurements . . . . .	45
Eight Hour Awake Measurements . . . . .	48
Eight Hours Awake Fed Secretions . . . . .	53
Eight Hours Awake Fasting Secretions . . . . .	53
Eight Hour Anaesthetized Measurements . . . . .	60
Eight Hours Anaesthetized Fed Secretions . . . . .	69
Eight Hours Anaesthetized Fasting Secretions . . . . .	69
II. Second Stage . . . . .	69
Group A . . . . .	70
Group B . . . . .	70
General . . . . .	70
DISCUSSION . . . . .	95
I. Twenty-Four Hour Studies . . . . .	95
II. Eight Hour Studies . . . . .	95
III. Possible Mechanisms of Gastric Hypersecretion Following	
Enterectomy . . . . .	97
Potentiation of Secretogogues . . . . .	97
Prolonged Gastric Emptying Time . . . . .	97
Liver Damage . . . . .	98
Infection . . . . .	98
Corticosteroids . . . . .	98





Intestinal Phase . . . . .	98
Removal of Inhibitors . . . . .	99
IV. Conclusions . . . . .	104

PART 2. EFFECTS OF MASSIVE ENTERECTOMY AND AN ANTIPERISTALTIC SEGMENT  
ON GASTRIC SECRETION

REVIEW OF THE LITERATURE ON REVERSED INTESTINAL SEGMENTS . . . . .	109
METHODOLOGY . . . . .	118
I. General . . . . .	118
II. Experimental Plan . . . . .	118
III. Before Operation . . . . .	119
IV. Operation . . . . .	119
V. Heidenhain Pouch Construction . . . . .	120
VI. Enterectomy . . . . .	120
VII. Segmental Reversal . . . . .	123
VIII. Postoperative Management . . . . .	125
IX. Collection of Samples . . . . .	126
X. Laboratory Procedures . . . . .	127
Determination of Gastric Acidity . . . . .	127
RESULTS . . . . .	129
I. Twenty-Four Hour Heidenhain Pouch Secretions . . . . .	129
Control . . . . .	129
After Massive Enterectomy . . . . .	129
After Segmental Reversal . . . . .	133
II. Eight Hour Awake Heidenhain Pouch Secretions . . . . .	133





	PAGE
Control . . . . .	133
After Massive Enterectomy . . . . .	134
After Segmental Reversal . . . . .	134
III. Eight Hour Anaesthetized Heidenhain Pouch Secretions. .	138
Control . . . . .	138
After Massive Enterectomy . . . . .	138
After Segmental Reversal . . . . .	138
IV. Body Weights . . . . .	142
V. Gastric Emptying Times . . . . .	142
Controls . . . . .	142
After Massive Enterectomy . . . . .	145
After Segmental Reversal . . . . .	145
DISCUSSION . . . . .	156
I. Increase in Gastric Secretion . . . . .	156
II. Increase in Transit Time . . . . .	157
III. Decline in Body Weight . . . . .	159
BIBLIOGRAPHY . . . . .	164



## LIST OF TABLES

PART 1. EFFECTS OF PROXIMAL VERSUS DISTAL ENTERECTOMY  
ON GASTRIC SECRETION

TABLE	PAGE
1. Mean Total Postprandial Heidenhain Pouch Secretions in Control Dogs, Dogs with 55% Proximal Enterectomy (Group A), and Dogs with 55% Distal Enterectomy (Group B). Volumes, Free Acid and Total Acid Concentrations are Shown, and the Statistical Significance of the Changes Following Enterectomy . . . . .	47
2. Mean Total Fasting Heidenhain Pouch Secretions in Control Dogs, Dogs with 55% Proximal Enterectomy (Group A), and Dogs with 55% Distal Enterectomy (Group B). Volumes, Free Acid and Total Acid Concentrations are Shown, and the Statistical Significance of the Changes Following Enterectomy . . . . .	49
3. Mean Total Eight Hourly Heidenhain Pouch Secretion in Awake Controls and Enterectomized Dogs, Fed and Fasting, and the Statistical Significance of the Changes Following Enterectomy . . . . .	56
4. Mean Hourly Heidenhain Pouch Secretions in Awake Dogs . . .	57
5. Mean Hourly Heidenhain Pouch Secretions in Awake Dogs Group A (Proximal Enterectomy) . . . . .	58
6. Mean Hourly Heidenhain Pouch Secretions in Awake Dogs Group B (Distal Enterectomy) . . . . .	59
7. Mean Total Eight Hourly Heidenhain Pouch Secretions in Anaesthetized Controls and Enterectomized Dogs, Postprandial and Fasting, and the Statistical Significance of the Changes Following Enterectomy . . . . .	65
8. Mean Hourly Heidenhain Pouch Secretions in Anaesthetized Dogs Controls . . . . .	66
9. Mean Hourly Heidenhain Pouch Secretions in Anaesthetized Dogs Group A (Proximal Enterectomy) . . . . .	67





## TABLE

## PAGE

10.	Mean Hourly Heidenhain Pouch Secretions in Anaesthetized Dogs Group B (Distal Enterectomy) . . . . .	68
11.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	77
12.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	78
13.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	79
14.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	80
15.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	81
16.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	82
17.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	83
18.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	84
19.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	85
20.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	86
21.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	87
22.	Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures . . . . .	88



## TABLE

## PAGE

23.	Hourly Heidenhain Pouch Secretion in Group A Dogs During Baseline Collections (Hours One and Two), Postprandial Collections with Thoracic Duct Lymph Diverted (Hours Three, Four, Five and Six), and Post Lymph, Reinfusion Collections (Hours Seven and Eight); and Mean Hourly Volumes and Acid Concentrations . . . . .	89
24.	Individual Hourly Heidenhain Pouch Secretion in Group B Dogs During Baseline Collections (Hours One and Two), Postprandial Collections with Thoracic Duct Lymph Diverted (Hours Three, Four, Five, and Six), and Post Lymph, Reinfusion Collections (Hours Seven and Eight); and Mean Hourly Volumes and Acid Concentrations . . . . .	90
25.	Comparison of Hours Seven and Eight with the First Six Hours of Secretion in the Thoracic Duct Diversion in Proximal Enterectomy . . . . .	91
26.	Comparison of Hours Seven and Eight with the First Six Hours of Secretion in the Thoracic Duct Diversion in Distal Enterectomy . . . . .	92
27.	Mean of the First Six Hours of the Thoracic Duct Diversion in Dogs with Distal Enterectomy Compared with the Mean of the First Six Hours of Duct Diversion in Dogs with Proximal Enterectomy . . . . .	93
28.	Mean of the Last Two Hours of the Thoracic Duct Diversion in Dogs with Distal Enterectomy Compared to the Last Two Hours of the Proximal Duct Diversion . . . . .	94

## PART 2. EFFECTS OF MASSIVE ENTERECTOMY AND AN ANTIPERISTALTIC SEGMENT

## ON GASTRIC SECRETION

1.	Mean Total Twenty-Four Hour Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). Statistically Significant Increases ( $p = 0.01$ ) were Noted in Heidenhain Pouch Secretory Volume, Free and Total Acid Concentrations, After Both Operative Procedures .	131
----	--	-----





## TABLE

## PAGE

2. Mean Total Twenty-Four Hour Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment. No Statistically Significant Change Following Enterectomy, but after Insertion of the Reversed Segment, Significant Changes were Noted in Heidenhain Pouch Secretory Volume, Free and Total Acid Concentrations . . . . . 132
3. Mean Total Eight Hour Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A) and Dogs with an Antiperistaltic Jejunal Segment (Group B). None of the Heidenhain Pouch Secretory Changes Following Either Procedure was Statistically Significant . . . . . 136
4. Mean Total Eight Hour Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). No Statistically Significant Secretory Change was Observed After Either Procedure . . . . . 137
5. Mean Total Eight Hour Anaesthetized Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). None of the Secretory Changes Following Either Procedure was Statistically Significant . . . . . 140
6. Mean Total Eight Hour Anaesthetized Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). None of the Secretory Changes Following Either Procedure was Found to be Statistically Significant . . . . . 141
- 1<sup>s</sup> Statistical Analysis of the Changes in Twenty-Four Hour Total Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3). . . . . 150



## TABLE

## PAGE

2 <sup>S</sup>	Statistical Analysis of the Changes in Twenty-Four Hour Total Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations in Control Dogs (E1), Enterectomized Dogs (E2), and Dogs with an Anti-peristaltic Jejunal Segment (E3) . . . . .	151
3 <sup>S</sup>	Statistical Analysis of the Changes in Eight Hour, Hourly Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Anti-peristaltic Jejunal Segment (E3) . . . . .	152
4 <sup>S</sup>	Statistical Analysis of the Changes in Eight Hour, Hourly Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3) . . . . .	153
5 <sup>S</sup>	Statistical Analysis of the Changes in Eight Hour Anaesthetized Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3) . . . . .	154
6 <sup>S</sup>	Statistical Analysis of the Changes in Eight Hour, Hourly Anaesthetized Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2), and Dogs with an Anti-peristaltic Jejunal Segment (E3) . . . . .	155





## LIST OF ILLUSTRATIONS

PART 1. EFFECTS OF PROXIMAL VERSUS DISTAL ENTERECTOMY  
ON GASTRIC SECRETION

FIGURE	PAGE
1. Heidenhain Pouch . . . . .	35
2. 55% Proximal Enterectomy . . . . .	37
3. 55% Distal Enterectomy , . . . .	39
4. Comparison of the Mean Twenty-Four Hour Postprandial Heidenhain Pouch Secretion in Control Dogs, and Enterectomized Group A and Group B Dogs. Secretion was Significantly Increased in both Groups ( $p = 0.05$ ). Free and Total Acid was Significantly Increased ( $p = 0.05$ ) in Group A Dogs, but not in Group B Dogs. . . . .	46
5. Comparison of the Mean Twenty-Four Hour Fasting Heidenhain Pouch Secretion in Control Dogs, and Enterectomized Group A and Group B Dogs. Secretion was Increased in Group A, and the Free and Total Acid was Increased in both Groups. None of these Increments was Statistically Significant . . . .	50
6. Comparison of the Mean Hourly Awake Postprandial Heidenhain Pouch Secretory Volumes of Control Group, Group A and Group B Dogs. Post Enterectomy, the Volume of Group A Secretions Diminished, and that of Group B Increased. Neither Change was Statistically Significant . . . . .	51
7. Comparison of the Mean Hourly Awake Postprandial Heidenhain Pouch Acid Concentrations of Control Dogs, Group A and Group B Dogs. Post Enterectomy, the Acid Level of Group A Diminished, and that of Group B Increased. Neither Change was Statistically Significant, . . . . .	52
8. Comparison of the Mean Hourly Awake Fasting Heidenhain Pouch Secretory Lumes of Control Group, Group A and Group B Dogs, Post Enterectomy, the Secretory Lumes of Both Groups Decreased Significantly ( $p = 0.05$ ) , . . . .	54



9. Comparison of the Mean Hourly Awake Heidenhain Pouch Acid Concentrations in Awake and Fasting Control Dogs, Group A and Group B Dogs. Post Enterectomy, in Group A There was a Significant Decrease in the Free Acid ( $p = 0.01$ ) and the Total Acid ( $p = 0.01$ ) and in Group B a Significant Decrease in the Free Acid ( $p = 0.01$ ) and the Total Acid ( $p = 0.05$ ) . . . . . 55
10. Comparison of the Mean Hourly Anaesthetized Postprandial Heidenhain Pouch Secretory Volumes of Control Dogs, Group A and Group B Dogs. Enterectomy had no Significant Effect on that of Group A, but Significantly Increased that of Group B ( $p = 0.05$ ). . . . . 61
11. Comparison of the Mean Hourly Anaesthetized Postprandial Heidenhain Pouch Acid Concentrations of Control Dogs, Group A and Group B Dogs. Enterectomy Significantly Decreased the Free and Total Acid Concentration in Group A ( $p = 0.05$ ), and Significantly Increased the Free and Total Acid in Group B ( $p = 0.05$ ) . . . . . 62
12. Comparison of the Mean Hourly Anaesthetized Fasting Heidenhain Pouch Secretory Volumes of Control Dogs, Group A and Group B Dogs. No Significant Changes Occurred Following Enterectomy . . . . . 63
13. Comparison of the Mean Hourly Anaesthetized Fasting Heidenhain Pouch Acid Concentrations of Control Dogs, Group A, and Group B Dogs. Enterectomy Produced a Significant Fall in Free and Total Acid Concentration in Group A ( $p = 0.05$ ) but no Significant Change in Group B Dogs. . . . . 64
14. Comparison of the Mean Hourly Heidenhain Pouch Secretory Volumes of Anaesthetized and Thoracotomized Group A and B Dogs. Feeding and Diversion of the Thoracic Duct Lymph had no Measurable Effect on Either Group. Reinfusion of Diverted Lymph Significantly Increased the Secretory Volume ( $p = 0.01$ ) of Group A Dogs, but had no Significant Effect on that of Group B Dogs . . . . . 71
15. Comparison of the Mean Hourly Heidenhain Pouch Acid Concentrations in Anaesthetized and Thoracotomized Group A and B Dogs. Feeding and Diversion of Thoracic Duct Lymph had no Measurable Effect in Either Group. Reinfusion of Diverted Lymph Significantly Increased the Free and Total Acid Concentration ( $p = 0.01$ ) in Group A, but had no Significant Effect in Group B . . . . . 72





## FIGURE

## PAGE

16.	Hourly Heidenhain Pouch Secretory Volumes in Anaesthetized and Thoracotomized Group A Dogs. Mean Volumes for the Two Hour Fasting, Four Hour Postprandial Lymph Diverted, and Two Hour Lymph Reinfusion Periods are Illustrated with a Dotted Line . . . . .	73
17.	Hourly Heidenhain Pouch Secretory Volumes in Anaesthetized and Thoracotomized Group B Dogs. Mean Volumes for the Two Hour Fasting, Four Hour Postprandial Lymph Diverted and Two Hour Lymph Reinfusion Periods are Illustrated with a Dotted Line . . . . .	74
18.	Comparison of Mean Heidenhain Pouch Secretory Volumes in Anaesthetized and Thoracotomized Group A and B Dogs for the Two Hour Fasting, Four Hour Postprandial Lymph Diverted, and Two Hour Lymph Reinfusion Periods . . . . .	76

## PART 2. EFFECTS OF MASSIVE ENTERECTOMY AND AN ANTIPERISTALTIC SEGMENT

## ON GASTRIC SECRETION

1.	Heidenhain Pouch . . . . .	121
2.	Massive Enterectomy . . . . .	122
3.	Insertion of an 8 cm. Antiperistaltic Segment . . . . .	124
4.	Effect of Enterectomy and Subsequent Insertion of an Antiperistaltic Segment, on Mean Total Twenty-Four Hour Postprandial and Fasting Secretion. Both Enterectomy and Reversal Significantly Increased Heidenhain Pouch Secretion in Postprandial Dogs ( $p = 0.01$ ) as Compared to the Controls. There was no Significant Increase in Heidenhain Pouch Secretion after Enterectomy in Fasting Dogs, but Reversal Resulted in a Significant Increase ( $p = 0.05$ ). . . . .	130
5.	Effect of Enterectomy and Subsequent Insertion of an Antiperistaltic Segment on Mean Total Eight Hour Heidenhain Pouch Secretory Volumes in Awake Dogs. No Significant Changes were Observed after Either Procedure as Compared to the Controls . . . . .	135
6.	Effect of Enterectomy and Subsequent Insertion of an Antiperistaltic Segment on Mean Total Eight Hour Heidenhain Pouch Secretory Volumes in Anaesthetized Dogs. No Statistically Significant Changes were Observed after Either Procedure . . . . .	139



## FIGURE

## PAGE

7. Comparison of the Mean Body Weights of Dogs Before Enterectomy, Two Months after Massive Enterectomy, and Two and Three Months after Reversal of a Jejunal Segment . . . . . 143
8. Barium X-rays of Control Dog's (1359) Gastric Emptying Time. The Plate on the Left Shows the Stomach a Few Minutes after the Dog had Swallowed the Barium Mixture. The Plate on the Right Shows the Same Stomach Empty Three Hours Later . . . . . 144
9. Barium X-rays of Dog 1359 after Enterectomy. The Plate on the Left Shows the Stomach a Few Minutes After the Dog had Swallowed the Barium Mixture. The Plate on the Right Shows the Same Stomach Empty Three Hours Later . . . . . 146
10. Barium X-rays of Dog 1359 after Insertion of an Anti-peristaltic Segment. The Plate on the Left Shows the Stomach a Few Minutes after the Dog had Swallowed the Barium Mixture. The Plate on the Right Shows the Same Stomach Remaining Partially Full Three Hours Later . . . . . 147
11. Barium X-ray of Dog 1359 after Insertion of an Anti-peristaltic Segment. The Stomach is Almost Empty of the Barium Mixture at Six Hours after its Ingestion, Demonstrating a Long Delay in Gastric Emptying After Segmental Reversal . . . . . 148



PART 1. EFFECTS OF PROXIMAL VERSUS DISTAL ENTERECTOMY  
ON GASTRIC SECRETION





REVIEW OF PHYSIOLOGICAL REGULATION  
OF GASTRIC SECRETION

Modern scientific study of gastric physiology begins with observations of secretions made on patients with gastric fistulae. In 1824, Doctor Beaumont (1) stopped trying to heal the wound in the abdomen of Alexis St. Martin, and concentrated on recording the intra-gastric happenings such as the change of color and contour with mood. Shortly after this, Bassov and Blondlot (2) described the production of gastric fistulae in dogs for experimental purposes, and from this time onwards, the detailed study of the working of the living stomach was no longer dependent upon fortuitous accidents. A. J. Carlson (3) reported on three such human patients in the nineteen twenties from his Chicago laboratory, and towards the end of World War II, Wolf and Wolffe (4) made extensive studies on the fistula of Tom Little.

At the turn of the century, the studies of Pavlov (5) began to indicate the complexity of the control of gastric secretion. The canine stomach was used as an experimental model from which various pouches could be fashioned, and a rapid accumulation of basic knowledge of its working began to take place. It is instructive to trace the chronological development of the discoveries in the three main mechanisms that are now thought to affect gastric secretion--vagal, antral and intestinal. This is not only the order in which they were discovered,



but also the order of their relative importance of their contribution to gastric secretion.

### I. Vagal Mechanism

Beaumont had been surprised to find that gastric juice would flow at the anticipation of food, just as emotions like anger or disgust would halt the flow. Other workers, such as Richet, (1878) (6), noted that the actual consumption of food was not necessary to produce a gastric secretion, but it was not until the turn of the century that Pavlov provided the explanation. He demonstrated the importance of the vagus nerves in mediating gastric secretion in his classical experiment with dogs in 1895.

From their laboratory, Ivan Pavlov and Mme. Schumann-Simonovskaja showed that gastric secretion was not solely a function of the digestive tract. They built up a conditioned reflex in the dog, in which the feeding was accompanied by the ringing of a bell during the period of reinforcement. Subsequent presentation only of the neutral stimulus was able to evoke the digestive response for a time, and it was this phenomenon that led Pavlov to give up his work on the digestive glands, and concentrate his efforts on the nervous system. Implicating the vagus nerve as the logical anatomical link between the two organs, he cut the oesophagus in the neck, and brought the two ends out as separate openings. Gastric juice would flow when the animal was "sham fed" through the mouth, even though the food would leave the oesophagus in the upper neck. The flow of gastric juice was often prolonged and copious, but was abolished when the vagi were





interrupted, demonstrating this to be the efferent pathway.

Changes in the colour and motility of the gastric mucosa under different psychical conditions have been subsequently recorded through the years by many workers, namely Carlson (1923), Uvnas (1942) (7), Wolf and Wolff (1943), and many others.

Experiments on patients under hypnosis, by Bennett and Venables in 1920 (8), gave rise to secretion of gastric juice at the suggestion of enjoyable food, and to inhibition of the flow at the mention of disgusting substances. Other investigators have demonstrated an impaired flow of gastric juice when food is served in an unappetizing manner,

The role of the vagus nerve in the release of gastrin has been extensively studied by Grossman (9). He reports that cholinergic reflexes mediate the release of gastrin in both the "cephalic" and "gastric" phase of gastric secretion. In the cephalic phase, reflexes are mediated solely by the vagi, and are of two kinds: (a) direct cholinergic stimulation of parietal cells, (b) cholinergic release of gastrin from pyloric gland cells. In the gastric phase, he claims that the same mechanisms occur, but are mediated both by the vagi and local intramural pathways. Evidence for the latter is furnished by Redford (10), who showed in 1962 that topical anaesthetics applied to the gastric mucosa prevented the gastrin release formerly provoked by local stimuli.

As the complex concept of the control of gastric secretion gradually becomes clearer, the notion of separate "phases" acting in



unison is losing ground, and being replaced by the idea of different mechanisms acting in harmony (11). There is an interweaving of secreting agents, and an interdependence of their machinery. Nevertheless, since it is technically feasible to ablate the action of the vagus nerve in toto, it is instructive to observe the changes in secretion both with and without this neurogenic influence. Bilateral truncal vagotomy results in a decreased secretion of gastric acid, and decreased gastric motility (12). But the inhibition of gastric juice produced by the presence of fat in the duodenum is unaffected by vagotomy. On the other hand, the response to endogenous gastrin in a vagally innervated pouch is reduced by about fifty per cent once this innervation is ablated, (Dragstedt, 1966), (13). The traditional response to gastrin and to Histamine has been shown to drop by about thirty per cent in vagotomized cats (Emas and Grossman, 1967), (14).

French (15) reported in 1953 that electrical stimulation of the anterior hypothalamus produces an increase in gastric secretion. This result was preventable by vagotomy, but not by adrenalectomy. Next, stimulation of the posterior hypothalamus resulted in delayed secretion; and this was prevented by adrenalectomy, but not by vagotomy. The first part of this experiment was repeated by Mason in 1967 (16), with similar results.

The error of considering the vagal contribution to be exclusively inhibitory or stimulatory is shown by the experiments of Dragstedt, Johnson, Singer, and Oberhelman in 1960 (17). Although truncal vagotomy was now accepted as a procedure for reducing gastric acid



secretion, these workers confirmed the findings of Storer et al (1952) (18) that cutting the vagi to the main stomach caused an increased Heidenhain Pouch acid output, and that vagotomy of the small intestine produced a smaller rise in Heidenhain Pouch secretion. The proposed explanation for these phenomena is the secondary stimulation of antral gastrin, or a gastrin potentiator, thus increasing the contribution of the hormonal phase.

Another example of vagally-stimulated gastrin release is seen in the gastric hypersecretion following insulin-induced hypoglycaemia. This hypersecretion is initiated by degrees of hypoglycaemia of about half the normal blood sugar level (e.g. about 40 mgm. %), while lesser degrees produce a mild inhibition of gastric secretion. Nyhus et al (19) have demonstrated a thirty-fold increase in free HCl in dogs two hours after the intravenous administration of ten units of insulin. Grossman (20), however, had shown a twenty-fold increase in free HCl in antrectomized and enterectomized dogs an hour after insulin administration. The former finding is probably an example of vagal release of gastrin since his extrinsically innervated antra were isolated from acid and from local mechanical and chemical stimuli, and yet produced a significant acid secretory response following vagal stimulation. After denervation by antroneurolysis, acid production by insulin-induced vagal stimulation ceased. The latter finding is a direct effect on the parietal cells of hypothalamic stimulation of the vagus nerve, since all the known sites of gastrin production have been extirpated. Grossman (20) also found that intra-arterial infusion of acetylcholine pro-





duced an acid secretory response in the fundus, after all known sites of gastrin production had been removed, inferring from this that the main mechanism of stimulation of acid secretion by vagal stimulation is a direct cholinergic action on the fundic glands, demonstrating again the overall complexity of the different agents at work, and the fallibility of regarding the mechanisms as separate entities.

## II. Antral Mechanism

One of the earliest observations made in connection with gastric physiology was that food in the stomach caused a rise in the secretion of gastric juice. Pavlov had demonstrated this both in waking and narcotized subjects. In 1906, Edkins (21) made an extract of antral mucosa which, when injected intravenously into dogs, produced a brisk rise in gastric secretion. Pavlov had shown that acid introduced into the duodenum acted as an inhibitor of gastric juice, and in 1910, Bayliss and Starling (22) demonstrated the same result by instilling acid into the pyloric antrum. There is no general agreement as to the mechanism by which these inhibitions are produced, but evidence exists that humoral mediation is responsible in the case of the duodenum, since duodenal acidification reduces secretion from vagally-denervated fundic pouches (23). Nerve reflexes involving the vagus have been implicated by Sircus (24) in reducing gastric secretion after duodenal acidification. The inhibition of gastric acid secretion produced by antral acidification had been thought to be the result of local action of the lowered pH on the antral mucosa, or



an indirect action via the vagal nerve to the stomach. In 1956, Harrison, Lakey and Hyde (25) proposed another mechanism--an antral inhibitory hormone. Like the intestine, the antrum was now known to be able to stimulate or inhibit the flow of gastric juices.

In 1920 Popielski (26), working with Edkin's extract, concluded that it was Histamine, demonstrating for later workers the actions of this drug on gastric secretion. His conclusion was based on this extract's powerful stimulation of gastric secretion, and for many years its true nature was in doubt. But it gradually became clear that Histamine, apart from having systemic side effects of constricting smooth muscle and producing bronchospasm, was less potent than Edkin's substance in stimulating the flow of gastric juice, and subsequent refinements of technique showed that although Histamine was usually present in these tissue extracts, the substance under discussion was not inactivated by Histaminase. It was found to be a true hormone, and was named gastrin by Edkins. Attention was now focused on the antrum as the source of this stimulator, and in 1925, Lim and McCarthy (27) removed the fundus of the stomach and performed a vagotomy in a series of dogs, leaving only the antrum in alimentary continuity. When these dogs were fed, there was a rise in gastric secretion. Food in the antrum was thus shown to be the normal stimulus for gastrin production, although subsequently a wide variety of different substances was seen to be effective in promoting a flow, including simple distension with a balloon. Duval and Price (28) reproduced this remarkable finding with the subject anaesthetized, but later Lim and Mozer





(29) were able to abolish it when the antrum was locally anaesthetized, suggesting the possible existence of a mechanical as well as a chemical pathway.

Further advances in this field came from the work of Gregory and Ivy (30). In 1941, they made separate transplants of antrum and fundic pouch, and were able to collect secretion from both when the dog was fed, thus establishing the criteria for a hormonal mechanism. Later in the year, they devised experiments which demonstrated that the release of gastrin is dependent on cholinergic nerve-endings in the antral mucosa.

The exact confines of the antrum have been ingeniously delineated in vivo by Bergstrom and Broom in Sweden, in 1964 (31) by the change in colour of pulverized litmus sprayed over the gastric mucosa following a systemic Histamine challenge. In view of the considerable individual variation in the boundary between fundus and antrum, this method is better tailored to the requirements of the individual than the suggestion made in 1963 by Ruding and Hirdes (32) that at least eighty per cent of the lesser curve be resected in an antrectomy, this being the limit of the antral tissue as determined histologically by them in thirteen stomachs.

In 1951, Dragstedt (33) showed that the inhibition of gastric secretion by acid in the stomach was contingent on contact between the acid and cells of the pyloric mucosa, and implied a local mechanism at the cellular level, mediated by pH. In 1960, some of the data produced in a cross-circulation experiment by Duval and Price (34) made it clear



that acid introduced into the antrum on one dog would depress the antral secretion of another dog with whom it is cross-circulating, the latter dog's antrum having previously been stimulated to secrete by gentle inflation of a previously placed antral balloon with 15-25 ml. of air. The following year, Thompson and Lerner, (35) in another cross-circulation experiment, confirmed this finding when, after irrigating one antrum with acid, they were able to diminish the secretion in another denervated Heidenhain Pouch.

Recent work has shown that gastrin has many actions, and these have been classified, for experimental purposes, into (a) those reproducible by small doses of exogenous gastrin, and (b) those reproducible by large intravenous doses of exogenous gastrin, these latter effects not being produced at all by endogenously released gastrin. One paradoxical and so far unexplained finding in this regard was that of Gillespie and Grossman in 1963 (36), who discovered that a very large dose of exogenous gastrin actually inhibited gastric secretion. Evidence was furnished in 1963 by Menguy (37) that canine antral mucus has a high concentration of gastric inhibitory substance, and that this concentration is increased by vagal denervation of the antrum. Fundic secretion was not found to have any inhibitory action, and canine saliva was found to be weakly inhibitory. In a recent assay (1967) (38), a pure form of gastrin (probably the physiologically active constituent) was synthesized from hog antral mucosa. This was found to have approximately the same effect on gastric secretion as has Histamine, without having the unwanted side effects of Histamine.



Schofield (39) has found that an alkaline pH in the pyloric antrum leads to an increased flow of gastric juice, as might be expected from the foregoing studies with acid in the same site. In 1965 he found that the acid response to meat extract in the antrum was abolished by the administration of Atropine, showing that cholinergic nerve endings in the antral mucosa are involved in the pathway, and reinforcing the views of other workers that maximal gastric secretion is dependent on vagal and antral stimuli working together in concert, and is not forthcoming if the activity of one of these mechanisms is impaired.

### III. Intestinal Mechanism

From the simple and direct experiments with gastric fistulae, it was known that meat extracts, bread, egg white, meat, milk and liver introduced into the stomach caused a rise in gastric secretion. In 1900, Le Conte (40) demonstrated a similar phenomenon from certain foods in the intestine, the mechanism of which remains incompletely explained today. At the same time Pavlov (41) was showing that the introduction of acid into the duodenum actually inhibited the flow of gastric juice, while Sokolov (42) was achieving the same result using gastric juice itself as the agent. The following year, Bayliss and Starling (43), with their isolation of secretin, showed that one of the actions of this hormone was to inhibit gastric secretion (while stimulating that of the pancreas). Secretin, they found, was liberated from the duodenal mucosa following the action of acid, fat, fatty acids,





amino acids or water on the stomach or intestine.

The inhibitory effect of fat in the duodenum on both gastric secretion and motility was next recognized, and in 1926 this was demonstrated by Farrell and Ivy (44) to be independent of the nerve supply. On the basis of further experiments which suggested that this chalone was secreted from the wall of the proximal small intestine, this hormone was named "enterogastrone" by Kosaka and Lim in 1933 (45). In 1928 a similar phenomenon was recorded by Ivy and Olberg, (46) when they noted a decrease in gastric secretion together with contraction of the gallbladder produced by a hormone which they called "cholecystokinin". This hormone was liberated as a result of contact with the upper intestinal mucosa of acid chyme, fats and their hydrolysates. Ivy claimed that cholecystokinin was formed and absorbed into the blood stream during intestinal digestion; but whether this hormone is sufficient to cause a physiologically significant depression of gastric secretion remains dubious, and the "search for a specific chalone in the duodenal mucosa must continue"--Sven Anderssen, 1967 (47).

The next twenty years saw numerous substances investigated which, when placed in the intestine, gave rise to an increased gastric secretion. Babkin (48) showed that the introduction of peptone (and other products of protein digestion) into the small intestine stimulated gastric secretion. Later, Beamer, in 1944 (49) showed that the presence of bile was necessary in the upper intestine before peptone-like substances in the same site would promote increased gastric secretion, and then only after a latent period of about two hours. Babkin also



showed that excessive administration of Vitamin D depressed gastric secretion; further studies revealed that this was due to the corresponding increase in the blood calcium level, and that variations above or below the normal range will reproduce this inhibition.

The isolation of Serotonin in 1952 (Erspamer and Asero) (50) provided a substance which would, *inter alia*, inhibit gastric secretion while stimulating gastrointestinal motility--Olsen and Gray (51); Black and Fisher, 1958 (52). While this was being done, Resnick (53) showed the occurrence of Serotonin in the duodenum and jejunum.

In 1963, Silen, Hein, Albo and Harper (54) from the University of California published the results of their work with the biliary apparatus on gastric secretion. They found that obstruction of the common bile duct led to gastric hypersecretion, which persisted and increased if the liver became irreversibly damaged, but returned to normal levels if the damage could be reversed. If one liver lobe only was obstructed, the gastric hypersecretion occurred, but returned to normal if the resultant cirrhotic lobe was resected. The possibility of a gastric secretagogue from a damaged liver was proposed.

Lerner and Thompson had suggested in 1963 (55) that Heparin was an inhibitor of gastric secretion. They discovered that the intravenous administration of 100 mgm. of Heparin to adult dogs resulted in uniform inhibition of Heidenhain Pouch secretion following the stimulus of a test meal, the average percentage inhibition of free HCl being 70%. In the same animals, the same dose of i/v Heparin resulted in an inhibition of Heidenhain Pouch secretion following Histamine stimula-



tion, the average percentage inhibition of free HCl this time being 33%. They concluded that the binding of Histamine by Heparin both in vitro and in vivo was the mechanism of this action. In a paper published in 1965, Schulte and Ellison (56) noted that Heparin, in a dose of 2 mgm. per Kgm. body weight, had no predictable effect on maximal Histamine-stimulated gastric secretion. But in February, 1966, Thompson, Lerner, Tramontana, and Miller (57) showed a convincing and statistically significant inhibition of gastric secretion in all its phases on intravenous infusion of 10,000 U.S.P. units of Heparin. They reported the following decreases in gastric secretion as compared with control subjects:

Antral phase; food stimulus.....	74%
Intestinal phase; good stimulus.....	71%
Cephalic phase; insulin stimulus.....	39%
Antral phase; acetylcholine stimulus.....	46%
Mecholyl secretion.....	44%
Secretion stimulation by exogenous histamine....	25%
Secretion stimulation by exogenous gastrin.....	40%

The possible mechanism suggested was the binding of Heparin with Histamine in vivo or by preventing mast cell degranulation, but the evidence for this is circumstantial. The paper concludes by saying that there is still no role known for Heparin in gastric physiology. Histamine had been proposed as the common stimulant to gastric secretion, and several interrelations between Histamine and Heparin intrigued Thompson and his colleagues.

By 1965, Gillespie and Grossman (58, 59), in a continuing series of experiments had confirmed the previously mentioned inhibitory effect on gastric secretion of cholecystokinin and secretion. His





further investigation of inhibitory mechanisms included data on duodenal acidification, originally noted by Pavlov to diminish gastric secretion. The effect of acid in different parts of the alimentary tract now came under closer scrutiny by Grossman and his associates (60). They observed that acid instilled into the jejunum actually increased the volume of gastric juice secreted, while acid instilled into the ileum had no measurable effect on it. A series of experiments followed (61) in which they: (a) excised the pyloric sphincter, (b) transplanted the mid-duodenum together with the biliary and pancreatic ducts into the jejunum, (c) excised the duodenal bulb, and (d) removed the duodenum distal to the bulb, all of which resulted in an increased gastric secretion. Only total duodenectomy was found to abolish the increase. Andersson and Nillson (62), in the same year, showed that to inhibit the flow of gastric juice, the acid must be instilled into the region of the duodenal bulb, the distal part of the duodenum being ineffective for this purpose. Acid reflux into the antrum may be the inhibitory mechanism in this instance.

In 1966, the effect of fat in the duodenum was reappraised by Dibler, Harkins and Nyhus (63). The resultant inhibition was explained by either inactivation of circulating gastrin, or by direct action on the parietal cells; and the inhibition was noted to be reversed by pancreatic duct ligation, opening up a new field of inquiry. Grossman (64) has shown that an operation for bile exclusion, draining the common bile duct to the exterior, decreased the output of a Heidenhain Pouch. Going one stage further, Chey and Lorber (65), after reproducing



this inhibition by diverting the pancreatic secretion (or by pancreatectomy), could restore the status quo by the instillation of fresh pancreatic juice into the duodenum.

The phenomenon of gastric hypersecretion following resection of the small intestine, established by Landor and Baker earlier in the year (66), now came under scrutiny by Osborne and his co-workers later in 1966 (67). Continuing experiments showed that the rise in gastric secretion is proportional to the amount of intestine resected; that the parietal cell mass proliferates to increase the amount of basal secretion, occasionally to the extent of requiring gastric aspiration to deal with it. In one series, Osborne found that resection of the distal half of the small intestine stimulated a greater secretion in a Heidenhain Pouch than did a proximal resection. Stimulants and inhibitors of gastric secretion from the intestine were discussed, but the mechanism remains elusive. Either an inhibitor was removed, or a secretagogue was produced. - But which?

A paper from Pennsylvania in July 1968 by Copeland, Miller, and Smith (68) has demonstrated once again significant increases in Heidenhain Pouch secretion after isolation of parts of the small intestine, the maximal increase being observed when the duodenojejunal segment was removed from the food stream. While emphasizing the complex nature of control of gastric secretion by the small intestine, they made the important observation that their measured increases were the same whether the isolated segment was left in situ as a mucous fistula, or removed entirely from the body. This is taken as evidence that the increase in gastric secretion is not produced by a secretagogue, but



rather by the removal of an inhibitor. Support for this view is given by Kerr, Elliott, and Endahl this year (69), who used the same methods to produce the same results in dogs. These experimental findings are at variance with a recent paper by Salmon and Wright (70) with human subjects, who showed a negligible rise in gastric secretion following massive small intestinal bypass in patients with obesity when the bypassed segment is left in situ as a mucous fistula, although the metabolic variation of these massively obese patients may invalidate any conclusion based on normo-somatic physiology.

Both of these views conflict with the findings of Westerheide, Elliott, and Hardacre (71), who, working from the same laboratory as Copeland, had shown in 1965 that an isolated and defunctionalized duodeno-jejunal segment resulted in a greater acid production than that obtained by excising the same segment. Thus a spectrum of results is available, the two extremes being directly opposed to each other.

The question of "secretagogue or inhibitor" remains under discussion. In a series of ten dogs provided with bypass of different portions of the small intestine, Copeland (72) described three with ileal exclusion. Two of these dogs satisfied the criteria for secretagogue release, namely an increase in the submaximal and maximal Histamine response postoperatively, but the third did not, and he concludes that, since attempts at extraction of such a substance have failed, its existence is "problematic". He notes that the animal's absorptive surface will have diminished, and that substances like calcium, and bile salts, which are known to affect gastric secretion,





and are absorbed through this surface, may play a role here by their relative absence. An interesting speculation here is the possibility of a decreased absorptive surface for an unknown substance having acid inhibitory potential.

Both the Pennsylvania group and Kerr's team from Columbus, Ohio (73) feel that it is the removal of an inhibitor that is responsible for the increase, mainly on the basis that identical hypersecretion is produced both by isolating and by excising the segment of small intestine. But the variability of this finding has already been mentioned.

On the other hand, more convincing argument in favour of a secretagogue comes from the paper of Yakimets and Bondar in 1967 (74). They found that the gastric hypersecretion following small bowel resection was reduced sharply on diverting the thoracic duct lymph--presumably the vehicle for the hormone--and restored on re-infusion of the lymph. Continuing this work, Chow (75) concluded that intact antral function was necessary for this phenomenon to occur, and that after resection of some 65% of small intestine, secretagogues are carried in the thoracic duct lymph from the retained small or large intestine, and may act by potentiating antral gastrin.

#### IV. Miscellaneous

Visceral.-- The part played by the pancreas remains imperfectly elucidated, although experimental work has shown some surprising results. Dragstedt (76) has produced duodenal mucosal ulceration in 100% of dogs



when he diverted their pancreatic ducts to the exterior, yet in 300 pancreatectomies in dogs the incidence of ulcer was only 1.3%. He rejects Mann's explanation that the corrosive action of the gastric juice on the duodenum is allowed to proceed without neutralization by the bicarbonate in pancreatic secretion, but admits the baffling nature of the phenomenon, since in both cases the pancreatic secretion is equally absent. Noting that a ligated pancreatic duct gives a 20% duodenal ulceration rate, "occupying the middle ground", he hypothesizes some mechanism, presumably hormonal, which acts as a stimulant to the production of acid gastric juice, the intact antrum not being necessary for this phenomenon to occur. This and similar observations by other investigators has led to the hypothesis that the external secretion of the pancreas has the characteristic of preventing mucosal ulceration, while its internal secretion may play a part in the production of intractable "stress" ulcer (Curling's; Cushing's ulcer).

Working on the assumption that gastrin may be partly destroyed or inactivated in the liver, Irvine and his associates (77) measured the Heidenhain Pouch secretion of animals before and after providing them with a portacaval shunt, and produced evidence in favor of this idea when he found the secretions raised postoperatively. His intact dogs were given doses of Histamine intra-jejunally that were insufficient to cause a raised Heidenhain Pouch secretion. This same dose was repeated following a portacaval shunt, when it produced a hypersecretion. One explanation is that Histaminase in the liver is bypassed by the operation; but in a subsequent editorial, Irvine (78) concludes that this is only



inferential, and that it is possible that the substance acting is gastrin. In 1960, Clarke (79) found that in human cirrhotics basal fasting and Histamine provocation tests were below normal in those without shunts, and not usually above normal in those with shunts. In the same year, a prospective study by Watkinson (80) revealed that in 20,000 post mortem examinations, the incidence of peptic ulcer was higher in human cirrhotics, suggesting another mechanism than gastric hypersecretion for its production.

Local factors.-- The chronic ingestion of gastric irritants may ultimately lead to lesions attributable to secretory changes. Bacteria, swallowed from chronic nasopharyngeal foci; alcohol; condiments and spices; thermal trauma from food and drink; and improper mastication are examples of such agents. Although cigarette smoking has been shown to hinder the healing of peptic ulcer, the mechanism is not yet clear. Tobacco-charged saliva is a gastric irritant, and the systemic effect of nicotine on the autonomic nervous system may produce gastric symptoms. Endoscopic proof of "tobacco gastritis", however, is not available.

Sundry drugs have been thought to produce gastritis, though in many cases the mechanism is obscure. Chief among the offenders are the salicylates and quinine derivatives. Extensive studies have convinced Menguy (81) and others that the effect of these drugs, and of corticosteroids, on the gastric mucosa, is due neither to a local effect, nor to an increased gastric secretion--on the contrary, in dogs they decrease the Heidenhain Pouch secretion--but to an impairment of the





ability of the gastric mucosa to form its protective layer of mucus. Douthwaite (82) has observed the gastric mucosa following aspirin ingestion, and seen a range of effects of the hemorrhagic type, with small ulcers containing fragments of the drug. He concludes that possibly the anticoagulant property of the drug may play a part. A similar picture may be produced experimentally by the introduction into the stomach of Cinchophen.

Other drugs implicated in the production of inflammatory and ulcerative lesions in the gastric mucosa are Phenylbutazone, Phenacetin, Indocid and others.

In a recent article from Japan, Tobe, Fujiwara, and Muryobayashi (83) have notes that the effect of Serotonin is to cause intense angio-spasm, muscular spasm and ulceration in rat and mouse stomachs; further studies on this substance are expected to yield information of clinical importance.

Work challenge.-- In 1960, Card and Marks (84) showed that the output of gastric juice is proportional to the number of parietal cells in the fundus. The notion that the number of these cells could vary in an individual was propounded by Landor in 1964 (85), when he produced a work hyperplasia of them by continued physiological stimulation, and showed further that this process is reversible. On the same track, Eraslan and Hardy (86) repeatedly injected slowly-released Histamine into dogs, over a period of seven weeks, with the result that all gained weight, hypertrophied their gastric mucosa, and underwent an increase in the number of parietal cells. Similar treatment with Hydrocortisone



led to a slight decrease in the number of parietal cells, and growth hormone appeared to have no effect.

In contrast, stomachs with a low acidity have been found to possess fewer parietal cells; this is seen in such diseases as carcinoma of the stomach, pernicious anaemia, chronic gastritis, acute fevers, malnutrition, gallbladder disease, Addison's disease, sprue, acne roseaceae and chronic arthritis.

It is the opinion of Dragstedt (87) that the protracted physiological challenge producing this hypersecretion is a persistence of the vagal mechanism acting at an inappropriate time which, if true, lends support to the theory of an "ulcer personality".

## V. Conclusion

As knowledge about gastric secretion accumulates, it is becoming increasingly clear that the traditional Pavlovian "phases" are not discrete. This structure would hinder the further understanding of this subject if rigidly imposed on the thinking since the phases do not work in isolation. The delicate interweaving of the different agents as they act on their target organ requires that they be understood in terms of each other, as well as in their own direct action on the stomach. In this way, such apparent paradoxes as the simultaneous stimulation and inhibition of secretion after vagal stimulation will be resolved, just as the duality of action of the antrum was understood by recourse to the other mechanisms.

As the traditional theory gives way to a new pattern of thinking, having served its purpose, so new practical methods replace the



time-honoured ones that have contributed so much information over the years. The sole method of collecting gastric secretions in the intact human subject has been by nasogastric aspiration of stomach contents, usually after a test meal. The value of this as an indication of regular intra-gastric events in the subject is limited, for the following reasons. In order not to block the aspiration tube, the test meal is usually liquid, whereas the normal human diet is a mixture of solid and liquid. Liquid alone takes a different intra-gastric course, and leaves the stomach more rapidly than a meal of solid food, thus stimulating its secretions for a different length of time.

The liquid in question must be free of protein, because protein will act as a buffer, and distort the pH. It must be fat-free, because fat in the duodenum depresses acid secretion; and the carbohydrates must be of a high molecular weight, and stable in the stomach, in deference to their osmotic capabilities.

S. J. Rune (88), in his current monograph from Copenhagen, has outlined these shortcomings, and shown that the customary test meal acts mainly as a volumetric stimulus, and is a weaker one than solid food. Moreover, since its emptying is exponential, the intra-gastric stimulus rapidly declines. Its inevitable lack of buffering capacity briskly leads to a high acid level in the antrum, which in turn artificially depresses gastrin release. Aspiration of the stomach contents for analysis gives only a spot reading, and concludes the test. Should other readings be required at different intervals following the test meal, the entire procedure must be repeated, and variables are introduced into the experiment.





Rune proposes a novel method of avoiding all these pitfalls, in which unlimited serial readings are taken after a realistic meal of solid food, without disturbing the stomach contents. The readings are taken from a fraction of the peripheral blood, and the principle behind the method is that acid lost from the parietal cells will alter the organism's acid/base balance proportionately. Base excretion in the urine and bicarbonate secretion from the pancreas are compensated for in the equation, which is simply: gastric acid secretion = net acid loss + base excretion in urine + pancreatic bicarbonate secretion.

Results with this indirect method have proved encouraging, and Rune's investigations have invariably shown an increase of the base concentration in arterial blood after the consumption of a major meal preceded by a twelve-hour fast in patients with normal gastric acid secretion. This increase was not found in patients with achlorhydria or low secretory capacity. It seems likely that more sensitive studies will be possible with this method as research continues in this field, where so many problems remain unsolved.



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## METHODOLOGY

### I. General

Adult mongrel dogs of both sexes and weighing 11 - 15 kg. were used. All animals were kept at the Health Sciences Animal Center, Ellerslie, Alberta, for two weeks before being released to the laboratory, during which time they were immunized with distemper vaccine, canine hepatitis vaccine, dewormed, and given any other special treatment necessary for the maintenance of good general health. Pregnant dogs were not used, and those which became ill or pregnant during the course of the experiments were excluded from the results.

The dogs were fed on commercial dog food<sup>\*</sup> according to size, the average being fourteen ounces per dog per day. Unrestricted water was supplied. The dogs were exercised daily in outdoor runs.

### II. Experimental Plan

Heidenhain Pouches were constructed on twelve dogs, and three weeks allowed for the recovery period before the secretions were measured repeatedly on all dogs under the following six sets of conditions.

1. Twenty-four hours fed, awake.
2. Twenty-four hours fasting, awake.
3. Eight hours fed, awake.
4. Eight hours fasting, awake.
5. Eight hours fed, asleep.
6. Eight hours fasting, asleep.

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\* Dr. Ballard's



Once this baseline was established, the dogs were divided into two groups of six--Group A, and Group B. Group A underwent resection of 55% of the small intestine just distal to the Ligament of Treitz, with end-to-end anastomosis (proximal enterectomy); Group B had 55% of the small intestine removed just proximal to the ileo-caecal valve, again with an end-to-end anastomosis (distal enterectomy).

After a recovery period of three weeks, Heidenhain Pouch secretions were again measured under the same six sets of conditions.

The final stage of the experiment was supra-diaphragmatic cannulation of the thoracic duct, diversion of its contents into a heparinized collecting vessel for four hours, followed by reinfusion of this lymph over the next two hours. After a thoracotomy, Heidenhain Pouch secretions were measured for two hours to establish a baseline. The anaesthetized dogs were then fed a measured quantity of food by orogastric tube (120 gm. of meat homogenized in 80 ml. distilled water), and the thoracic duct lymph simultaneously diverted for the next four hours. This lymph was reinfused into a systemic vein for the following two hours, at the end of which time, the animals were sacrificed. This procedure was carried out on the dogs of both groups.

### III. Before Operation

The animals were exercised normally up to the day of operation. Twenty-four hours of fasting from food and twelve from water preceded the operation. If examination of the animal before operation showed any abnormality, the procedure would be delayed until it was remedied; or the dog excluded from the series.



#### IV. Operation

The animals were anaesthetized with intravenous Nembutal, ("Diabutal") 30 mg./kg. body weight, and intubated with a cuffed endotracheal tube. The hair was shaved from the abdomen, and the underlying skin washed with surgical soap and water. The dog was then placed in the supine position on the operating table, where the legs were secured by a tether from each corner of the table and an intravenous solution of 5% dextrose saline started at 5 ml./kilo./hour. The operative site prepared with "Betadine" iodine solution. For the intra-abdominal procedures, a midline incision was used to facilitate a relatively bloodless entry; this was placed cephalad for Heidenhain Pouch construction, and more caudad for the enterectomies. Strict asepsis was maintained at all times.

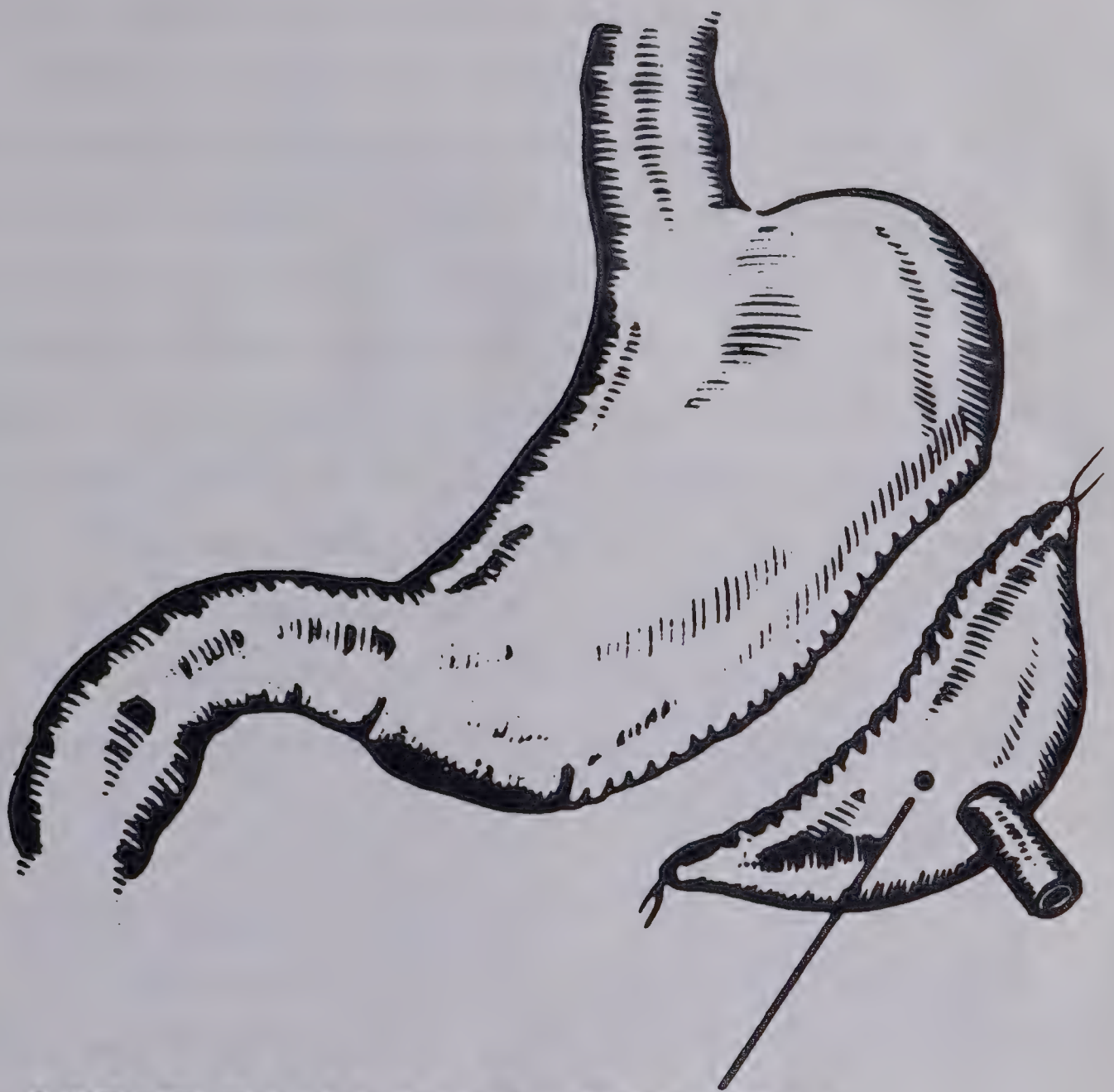
#### V. Heidenhain Pouch Construction (Figure 1)

After suitable preparation, the abdomen was opened, and a survey made of the tissues to exclude any pathological condition. If the spleen was large and bulky, it was exteriorized in moist sponges, to facilitate exposure and delivery of the stomach.

Gentle traction caudad on the greater curvature of the stomach permitted its delivery into the wound, where it was stretched out and flattened. The omentum was gently lifted off the upper surface, and non-crushing clamps applied in such a way as to isolate a large wedge of the organ from the greater curvature. The wedge was fashioned from the tissue of the proximal fundus, to avoid including significant amounts of antral mucosa. The point of the wedge was not allowed to







## HEIDENHAIN POUCH

Fig. 1.--Heidenhain Pouch



approach the lesser curvature too closely, to avoid producing a constriction in the body of the remaining stomach.

Before the clamps were removed from the main stomach, the cut edges of mucosa were joined with 3-0 chromic catgut, and this suture line buried with another 3-0 chromic catgut in the serosal layer. Before closure of the pouch, a stainless steel cannula was inserted, and brought out through a stab-wound away from the suture line. The cut edges of the pouch were then sewn together in the same way as those of the stomach, and the end of the cannula brought out through a stab-wound in the abdominal wall. The pouch was fixed in this position by several sutures between serosa and the tissues of the internal abdominal wall. Thus, pouch contents could be collected by applying a bag to the exteriorized part of the cannula, which would drain gastric secretions continuously.

#### VI. Proximal Enterectomy (Figure 2)

The total length of the small intestine, exteriorized on moist sponges, was measured with a ruler, the average being 300 cm. from the Ligament of Treitz to the ileocecal valve.

Measurement of the length to be resected was started at a point 5 cm. distal to the Ligament of Treitz. Markers were applied both here and at a point about 165 cm. (i.e. 55%) distal to this, delineating the amount to be resected, and non-crushing clamps were applied to the bowel wall at these points. The mesenteric vessels lying between these two points were ligated in continuity with 4-0 silk and divided between the ligatures. The intermediate intestine was then resected, to include



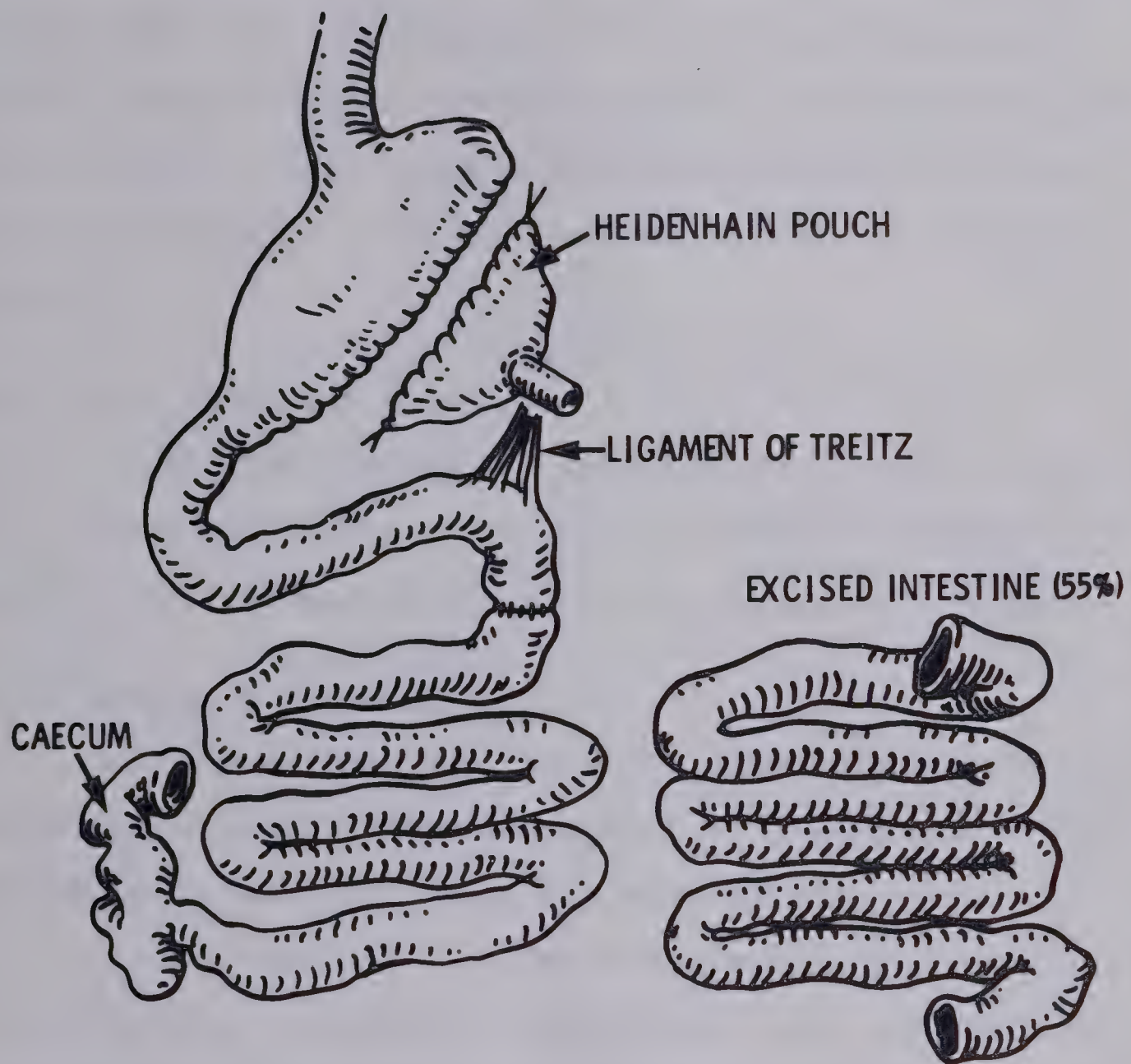


Fig. 2.--55% Proximal Enterectomy





the cuff that was clamped and continuity restored with a two layer end-to-end anastomosis, 5-0 chromic being used for the mucosa and 4-0 silk for the serosa. The mesenteric defect was then closed with 4-0 chromic sutures to prevent subsequent herniation. The abdominal wound was then closed in layers using an absorbable subcuticular stitch for the skin to obviate the need for suture removal during the recovery period.

#### VII. Distal Enterectomy (Figure 3)

The procedure used for this operation differed from that used for a proximal enterectomy only in that the resected intestine was measured cephalad from a point 5 cm. proximal to the ileocecal valve.

#### VIII. Thoracic Duct Cannulation

After endotracheal intubation with a cuffed tube which was then connected to a positive pressure ventilator, an intravenous solution of 5% dextrose saline was started at 5 ml./kilo./hour.

A right-sided thoracotomy was then performed with the dog lying on his left side. Exposure was maintained with a rib retractor, and the right lung was packed out of the field with moist sponges. Simultaneously with the thoracotomy, a Bard rubber bladder was attached to the cannula from the Heidenhain Pouch, and secretions measured hourly for two hours to establish a baseline before any further surgery was undertaken.

At the end of this two hour period, an incision was made in the parietal pleura overlying the aorta, and the thoracic duct identified as it lay in the dorsal sulcus alongside. The duct was ligated at its



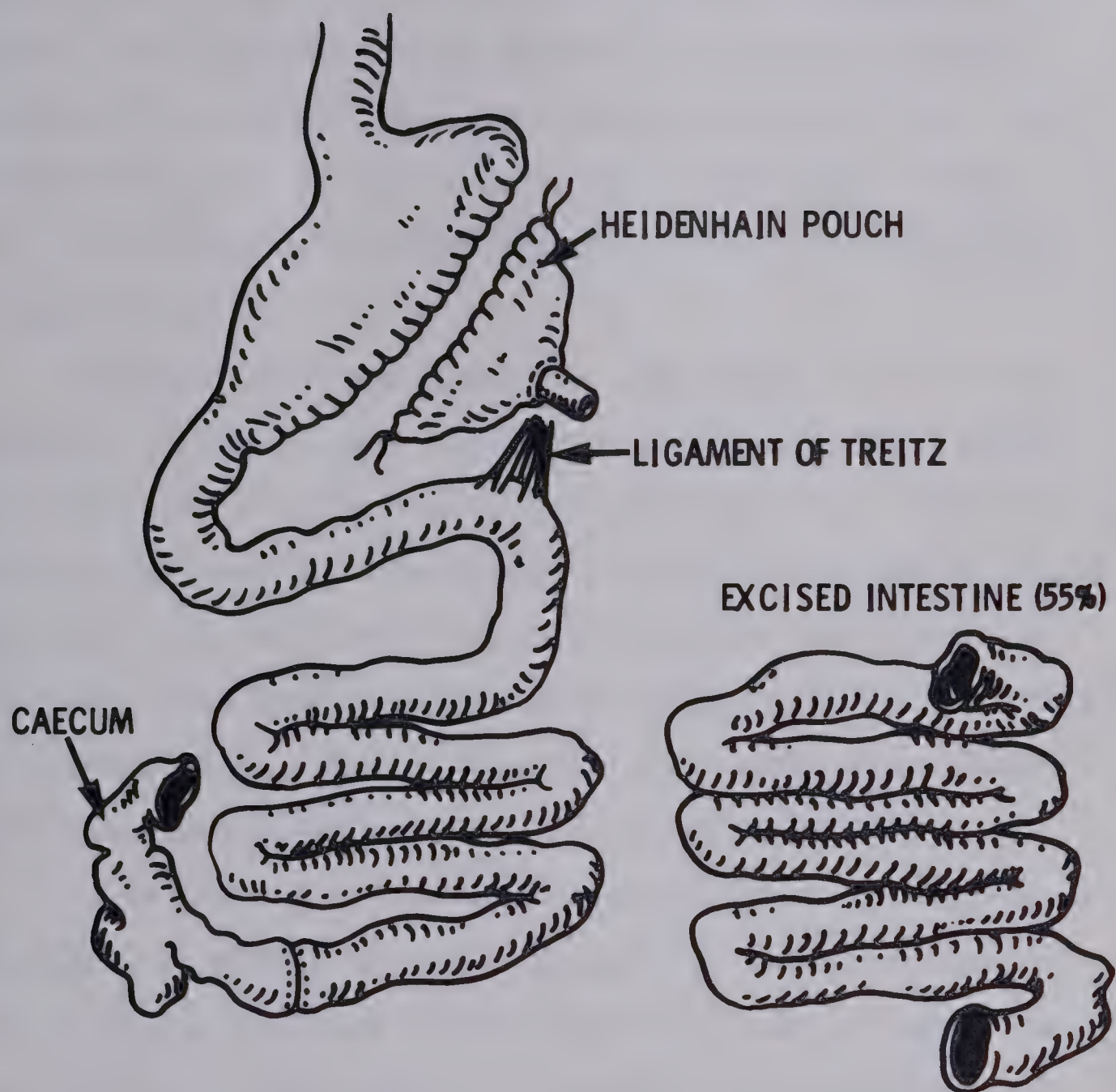


Fig. 3.--55% Distal Enterectomy



cephalad end in the field, to suffuse it with lymph and increase its calibre, and a silastic catheter threaded into it through a small incision. The catheter was passed caudally for its tip to lie in the cisterna chyli. At the same time the dog was fed 120 gm. of meat (Dr. Ballard's dog food) homogenized with 80 ml. of distilled water, through an orogastric tube,

The open end of the catheter was then brought out of the chest wound, and allowed to drain into a sterile graduated cylinder placed on a lower level than the chest to obtain a siphon effect. The rib retractor and packs were then removed, and the wound temporarily closed with towel clips and a sterile cover. Five hundred units of Heparin were added to the lymph draining into the cylinder to prevent clotting, and hourly recordings made of the volume of the lymph in the cylinder, and the Heidenhain Pouch secretions in the bag.

Four hours after the start of this collection, the intravenous infusion of 5% dextrose saline was stopped. An intravenous infusion was simultaneously started with this collected lymph, infused at the same rate over the next two hours. Measurements of Heidenhain Pouch secretion were continued in the same way. At the end of this two hour period, the procedure was terminated and the dog sacrificed.

#### IX. Postoperative Management

Parenteral fluids were given for three days following surgery, as 30 ml./kg. of 5% dextrose saline intravenously for the first day, and subcutaneously for the next two. After the third day the dog was permitted to drink water, then milk and pabulum or Heinz clear consomme of soup for two days. By the sixth day the dog was invariably back on





a normal diet,

Parenteral antibiotic was used prophylactically during surgery, and the immediate postoperative period, as 2 ml. of "Fortimycin" (a mixture of 400,000 I.U. penicillin and 0.5 gm. dihydrostreptomycin). The first dose was given on the morning of the surgery, and then daily until the third postoperative day. Normal exercise was resumed at this time.

Following enterectomy, the dog was given 1 gm. of calcium carbonate orally when normal feeding was resumed, to avoid problems of diarrhea. This has been shown to be due to the detergent property of the soaps irritating the intestinal mucosa. The insoluble calcium soap is precipitated, restoring the physiological nature of the luminal content. Negligible absorption of calcium takes place in the shortened intestine, and no hypercalciuria has been shown in animals fed up to 30 gm. of calcium (1). A minimum period of three weeks was allowed between the conclusion of the surgery and the beginning of any further measurements of Heidenhain Pouch secretion,

No special therapeutic measures, such as transfusion, were necessary during the postoperative period,

#### X. Collection of Samples

For the twenty-four hour collections the bladders were fitted on at 5:00 p.m. on one day, and removed with the secretions at 5:00 p.m. on the next. Normal activity was permitted during this period, with the exception that the dogs were muzzled to avoid their damaging the bladders. For the fed collections the muzzles were removed to allow the dogs to eat; and then replaced.



The food consisted of eight ounces of commercial dog food given twice daily; for the fasting collections only water was given as required.

For the eight hour collections, the same techniques were used on the conscious dogs, except that the collections were measured hourly. For the sleeping collections the animals were anaesthetized with intravenous Nembutal ("Diabutal") 30 mg./kg., and an endotracheal tube inserted. They were laid on their left side with the cannula and rubber bladder dependent, and intravenous 5% dextrose saline infused at a rate of 5 ml./kg./hr. Heidenhain Pouch secretions were collected and measured hourly. In the anaesthetized fed collections, 120 gm. of commercial dog meat was homogenized with 80 ml. of water, and given through an oro-gastric tube at the end of the second hour.

In all collections, the bladders were carefully inspected for any damage or leakage, and that collection discarded if any were discovered.

#### XI. Determination of Gastric Acidity

The volume of every sample was first measured and recorded. The amount of free and total acid in the secretions was determined for every sample by the following method: one milliliter of the sample was pipetted into a titration vessel in an autoburette, and the pH measured automatically and indicated on a pH meter,

The radiometer automatic titrator was then connected to the autoburette, and N/10 sodium hydroxide automatically added to the sample until a pH of 4.0 was reached, at which time the amount of free acid was indicated on a dial on the autoburette.



At this point another circuit was set in operation, which continued the titration to pH 7.0 when the amount of total acid appeared on the same scale on the autoburette.

No indication was used, because the amount of N/10 sodium hydroxide added to bring the pH to four and seven respectively was directly proportional to the amounts of free and total acid present.





## FOOTNOTES

<sup>1</sup>LeVEEN, H.H., BOREK, B., AXELROD, D.R., and JOHNSON, A.  
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intestine. Surg. Gyn. Obst., 124:766, 1967.



## RESULTS

### I. First Stage

Control values of Heidenhain Pouch secretion were established on twelve dogs, under the following conditions:

1. Twenty-four hours awake fed        )
2. Twenty-four hours awake fasting )       (one collection)
3. Eight hours awake fed                )
4. Eight hours awake fasting            )
5. Eight hours anaesthetized fed        )       (hourly collections)
6. Eight hours anaesthetized fasting    )

Six of these dogs subsequently underwent a 55% proximal enterectomy (Group A), and the remaining six a 55% distal enterectomy (Group B). Heidenhain Pouch secretions were again measured under identical conditions. These were examined for volume, pH, concentration of total acid, and concentration of free acid. In order to avoid giving a falsely high impression of the gastric acidity of dogs with a small Heidenhain Pouch secretion, the acidity is expressed in units of m.Eq./volume rather than m.Eq./litre.

#### Twenty-Four Hour Measurements

After enterectomy, both groups secreted a greater volume of gastric juice and acid when fed than the controls (Figure 4). Group A showed a 73% increase in volume, and Group B, a 66% increase (Table 1). Both these increases were statistically significant<sup>\*</sup> at 5% ( $p = 0.05$ ) (Tables 11 and 12).

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<sup>\*</sup> Statistical analysis (Tables 11-28) appear at the end of this section.



# MEAN 24 HR. POST PRANDIAL HEIDENHAIN POUCH SECRETION

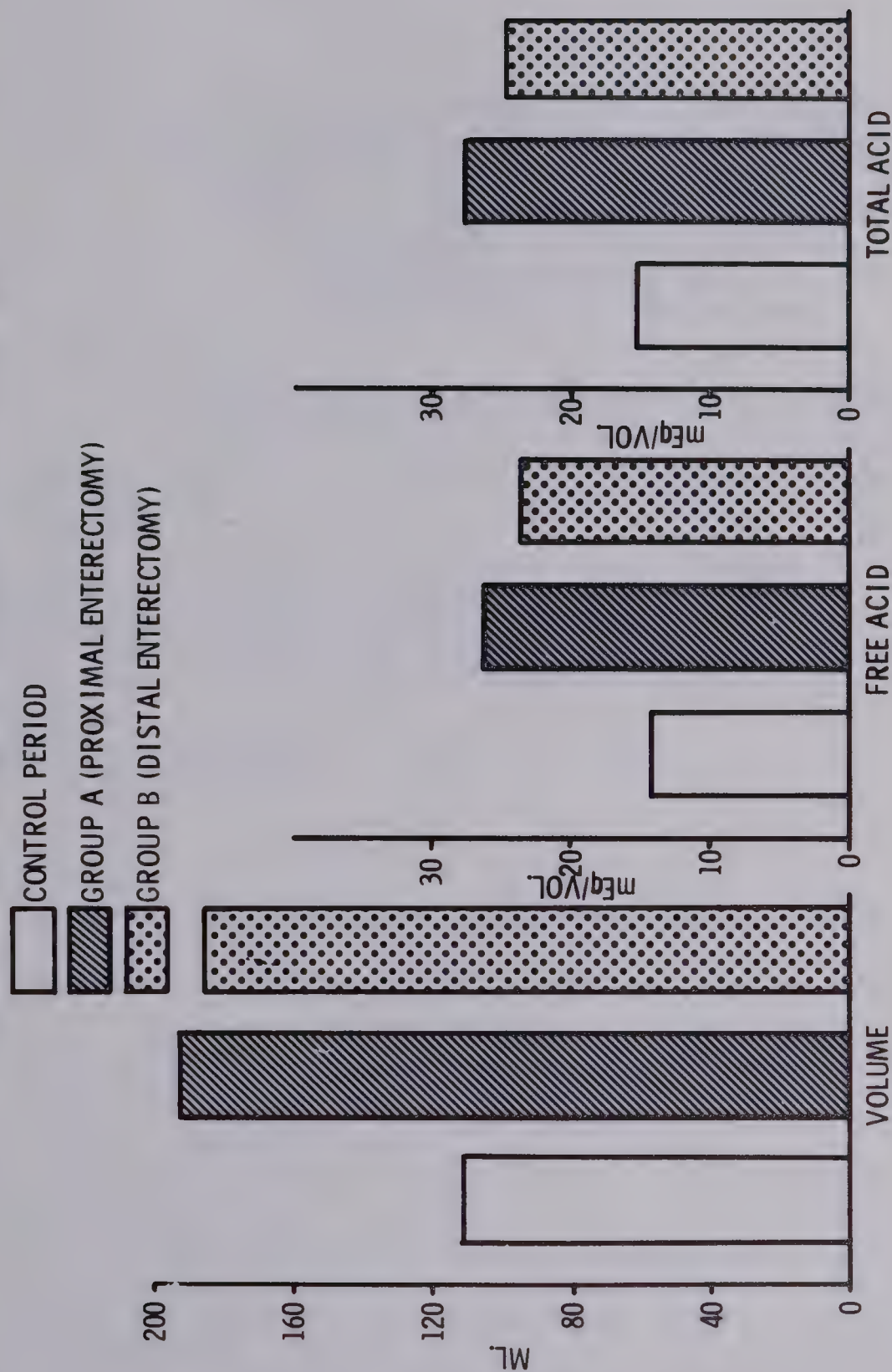


Fig. 4.--Comparison of the mean twenty-four hour postprandial Heidenhain Pouch secretion in control dogs, and enterectomized Group A and Group B dogs. Secretion was significantly increased in both groups ( $p = 0.05$ ). Free and total acid was significantly increased ( $p = 0.05$ ) in Group A dogs, but not in Group B dogs.





TABLE 1.--Mean Total Postprandial Heidenhain Pouch Secretions in Control Dogs, Dogs with 55% Proximal Enterectomy (Group A), and Dogs with 55% Distal Enterectomy (Group B). Volumes, Free Acid and Total Acid Concentrations are Shown, and the Statistical Significance of the Changes Following Enterectomy

	Control	Group A	P value	Group B	P value
24 hours fed					
Volume <sup>*</sup>	111.33	193.54	0.05	185.08	0.05
Free Acid <sup>†</sup>	14.26	26.62	0.05	23.96	N.S.
Total Acid <sup>†</sup>	15.59	27.73	0.05	25.09	N.S.

\* Volume in ml.

† Acid in m.Eq./volume.



In the fasting state, only Group A showed a greater volume of gastric juice than the controls, of 66% (Table 2). In Group B, the volume was unchanged as compared with the controls, though the acidity was almost doubled (Figure 5). None of these changes was statistically significant (Tables 13 and 14).

The effect of feeding was to increase the secretions of all dogs, including the controls.

The twenty-four hour collections were made during the weekends, when activities in the animal house were at a minimum. The dogs were not disturbed except for feeding and exercise, and the only time the collecting bags were emptied was at the end of the twenty-four hour period. Fewer extraneous stimuli were acting on the dogs during this time, a high proportion of which time was spent asleep. These factors may account for the relatively high hourly secretion compared with the eight hour hourly collections taken during the working week.

#### Eight Hour Awake Measurements

With the animals awake, and therefore subject to numerous external stimuli, no sustained nor significant pattern of Heidenhain Pouch secretion was evident.

When fed, Group A produced slightly less Heidenhain Pouch secretion than the controls (Table 15), while Group B showed a 60% rise (Table 16). Neither change was statistically significant. In all three groups, a steep rise in Heidenhain Pouch secretion occurred during that hour that followed feeding (Figures 6 and 7).



TABLE 2.--Mean Total Fasting Heidenhain Pouch Secretions in Control Dogs, Dogs with 55% Proximal Enterectomy (Group A), and Dogs with 55% Distal Enterectomy (Group B). Volumes, Free Acid and Total Acid Concentrations are Shown, and the Statistical Significance of the Changes Following Enterectomy

	Control	Group A	P value	Group B	P value
24 hours fasting					
Volume *	73.83	123.45	N.S.	73.08	N.S.
Free Acid †	5.08	13.15	N.S.	9.56	N.S.
Total Acid †	5.64	14.35	N.S.	10.44	N.S.

\* Volume in ml.

† Acid in m.Eq./volume.





# MEAN 24 HR. FASTING HEIDENHAIN POUCH SECRETION

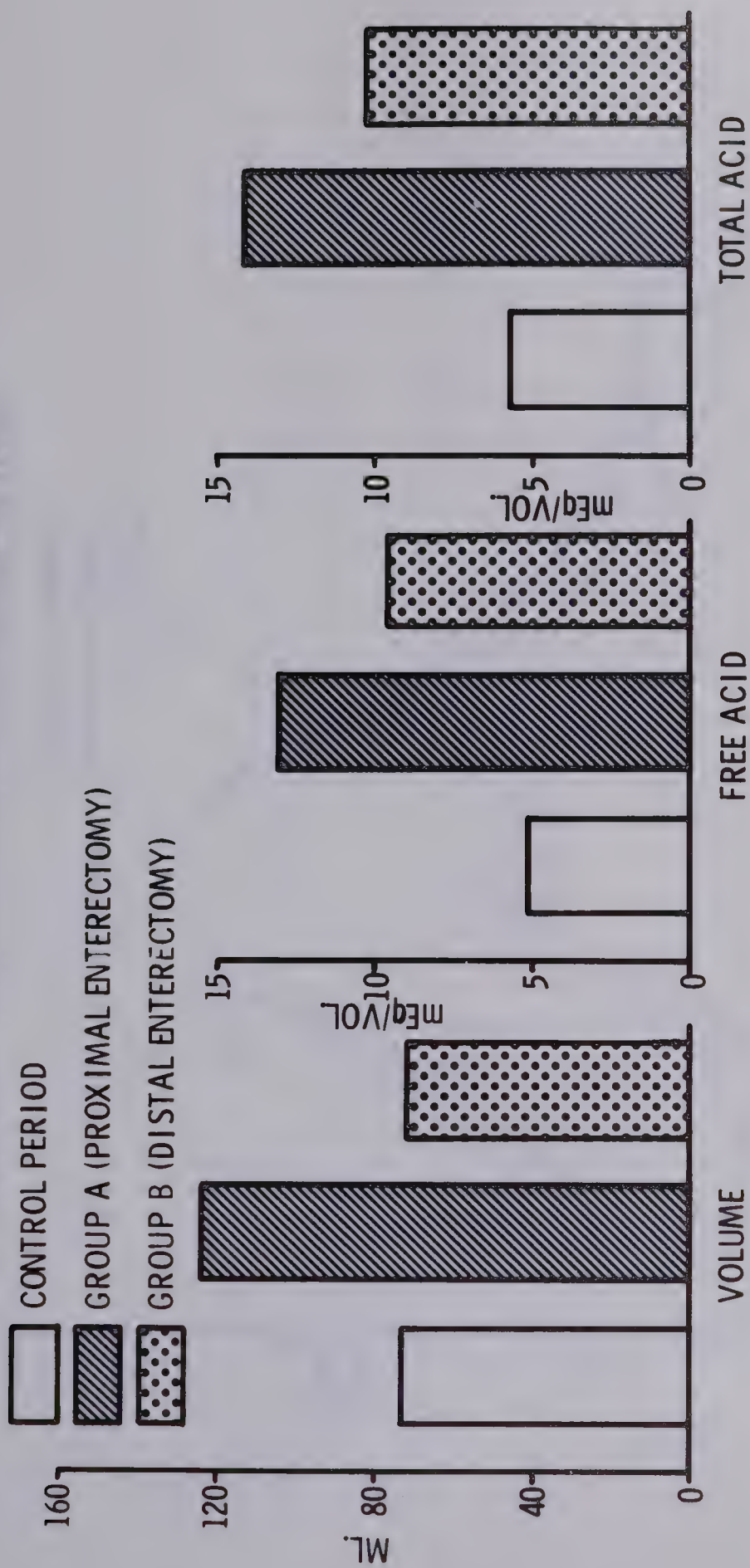


Fig. 5.--Comparison of the mean twenty-four hour fasting Heidenhain Pouch secretion in control dogs, and enterectomized Group A and Group B dogs. Secretion was increased in Group A, and the free and total acid was increased in both groups. None of these increments was statistically significant.



# MEAN 8 HR. AWAKE POST PRANDIAL HEIDENHAIN POUCH SECRETION

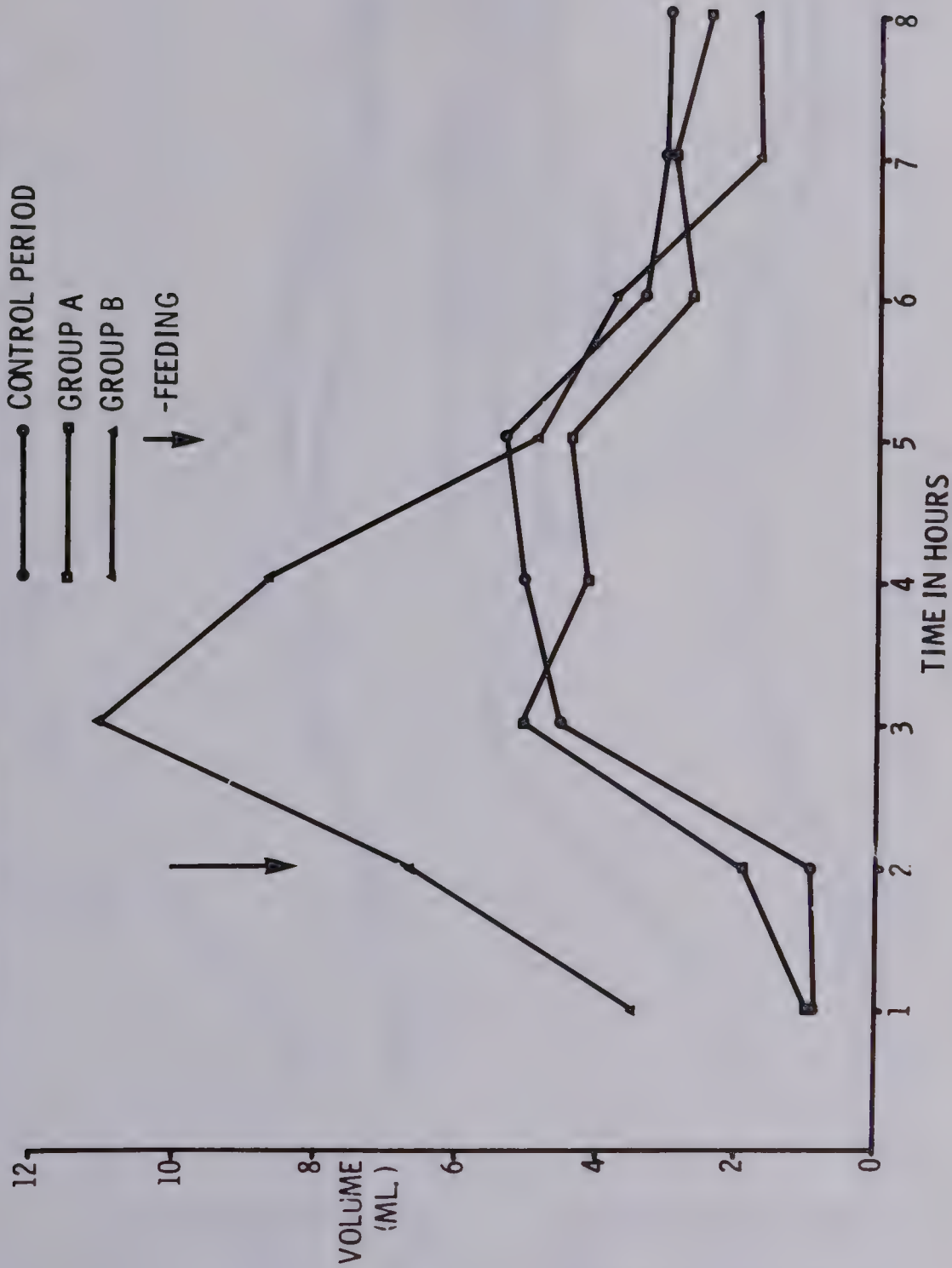


Fig. 6.--Comparison of the mean hourly awake postprandial Heidenhain Pouch secretory volumes of control group, Group A and Group B dogs. Post enterectomy, the volume of Group A secretions diminished, and that of Group B increased. Neither change was statistically significant.



# MEAN 8 HR. AWAKE POST PRANDIAL HEIDENHAIN POUCH SECRETION (2)

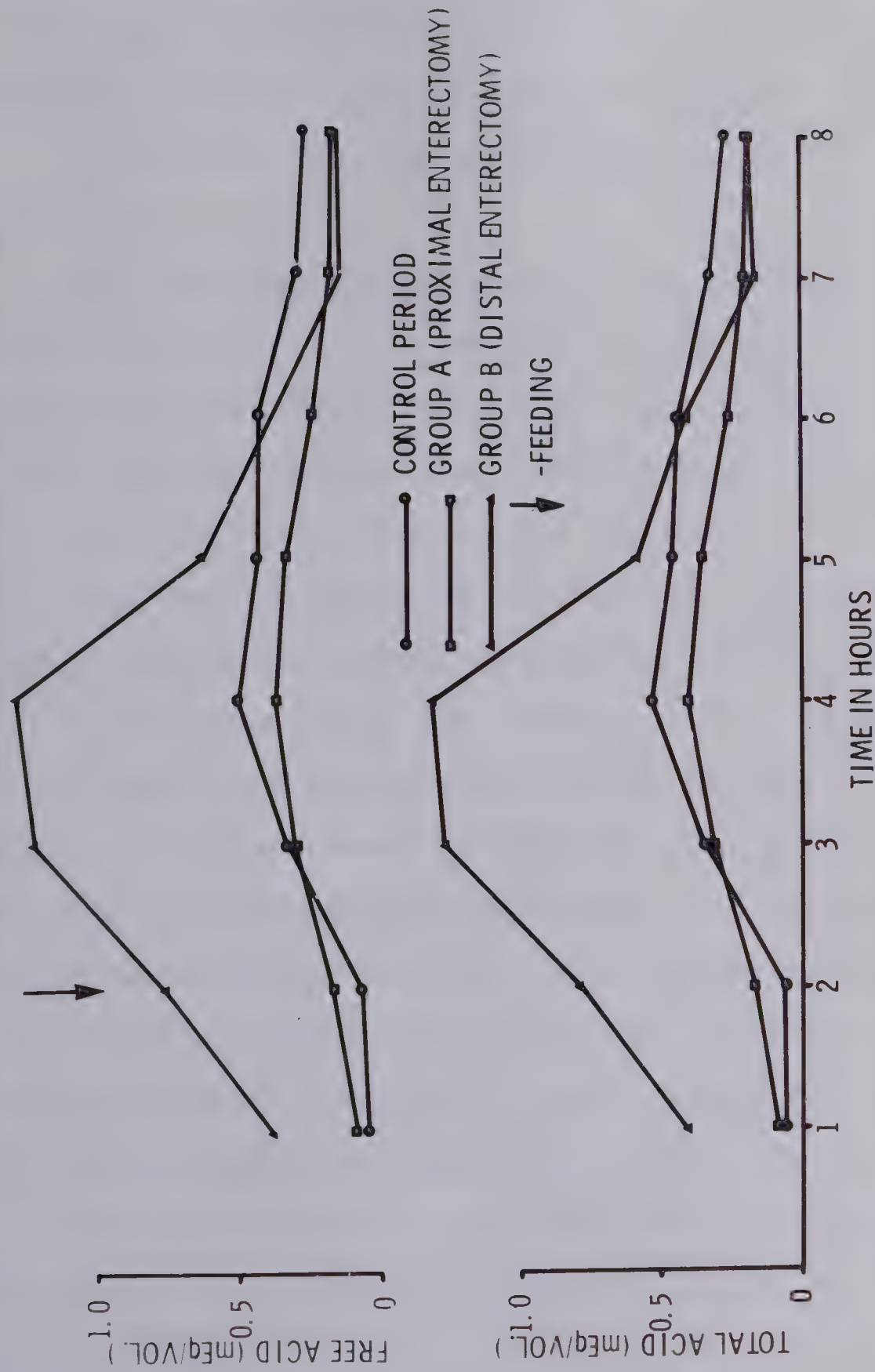


Fig. 7.--Comparison of the mean hourly awake postprandial Heidenhain Pouch acid concentrations of control dogs, Group A and Group B dogs. Post enterectomy, the acid level of Group A diminished, and that of Group B increased. Neither change was statistically significant.





In the fasting state, the decrease in Heidenhain Pouch secretions of both Groups A and B was apparent (Tables 17 and 18) and significant ( $p = 0.05$ ), and the diurnal variation of the gastric secretion of the fasting dog is well shown by the control group (Figures 8 and 9).

In both groups, the dogs secreted more when fed than fasting. (Tables 3, 4, 5, and 6).

Eight hours awake fed secretions.-- The general pattern of secretion was similar for the controls and both groups: after the baseline secretion was established over the first two hours, there was a fourfold rise after feeding for the next two hours, followed by a gradual decay over the last four hours of collection.

One interesting observation on the rate of change of gastric secretion: although the controls and both groups were fed in the same way, at the same times of day, both the rise and fall in gastric juice production from Group B was considerably faster than that of the other two groups. The steep increase in Heidenhain Pouch secretion in Group B after feeding was matched by a steep decline later, so that the collection at the eighth hour amounted to less than that taken at the first hour. This latter phenomenon occurred in three out of four conditions of collection in Group B, and never in either of the other groups, which rose to a lesser height, and sustained a more gradual decay.

With the dogs awake and fed, the gastric hypersecretion that follows massive enterectomy was not observed in Group A, but was present in Group B.

Eight hours awake fasting secretions.-- The diurnal variation of gastric secretion without a food stimulus is shown in this category.



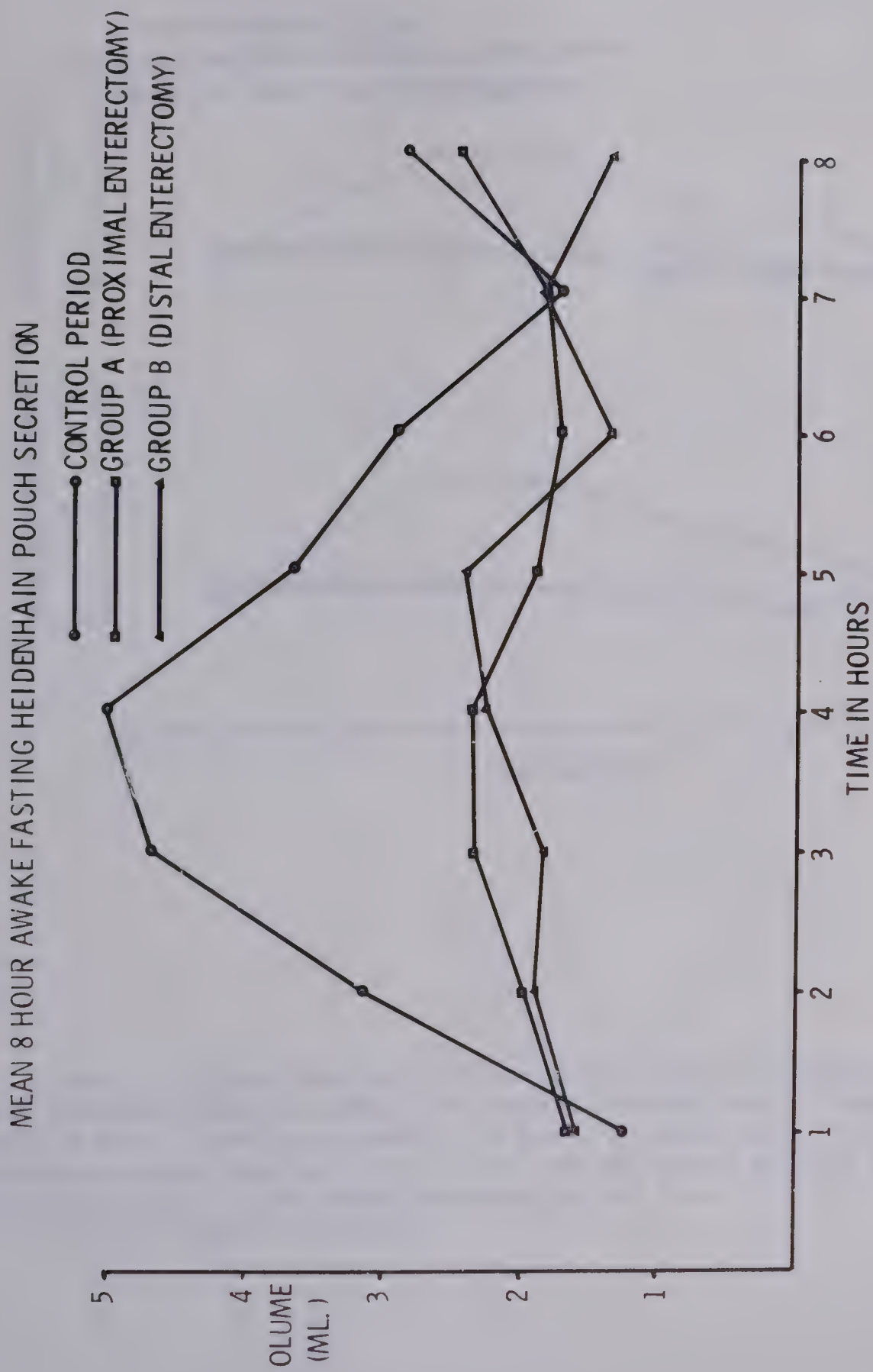


Fig. 8.--Comparison of the mean hourly awake fasting Heidenhain Pouch secretory volumes of control group, Group A and Group B dogs. Post enterectomy, the secretory volumes of both groups decreased significantly ( $p = 0.05$ ).



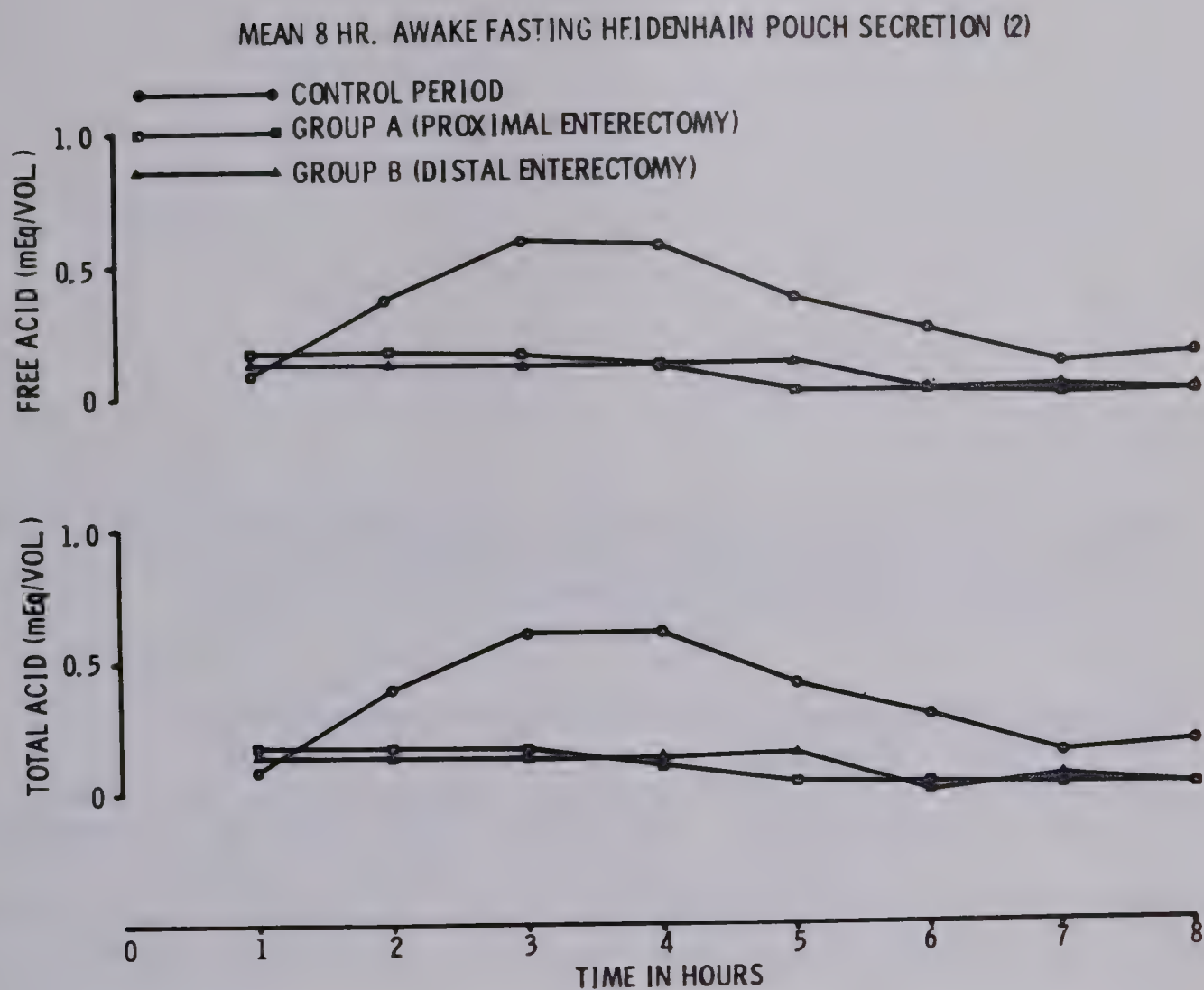


Fig. 9.--Comparison of the mean hourly awake Heidenhain Pouch acid concentrations in awake and fasting control dogs, Group A and Group B dogs. Post enterectomy, in Group A there was a significant decrease in the free acid ( $p = 0.01$ ) and the total acid ( $p = 0.01$ ) and in Group B a significant decrease in the free acid ( $p = 0.01$ ) and the total acid ( $p = 0.05$ ).





TABLE 3.--Mean Total Eight Hourly Heidenhain Pouch Secretion in Awake Controls and Enterectomized Dogs, Fed and Fasting, and the Statistical Significance of the Changes Following Enterectomy

	Control	Group A	Group B	Statistical significance
Postprandial	26.22 ml.	24.46 ml. N.S.	41.96 ml.	N.S.
Fasting	25.10 ml.	16.27 ml. $p = 0.05$	14.70 ml.	$p = 0.05$



TABLE 4.--Mean Hourly Heidenhain Pouch Secretions in Awake Dogs

## Control

	Hours							
	1	2	3	4	5	6	7	8
Dogs fed at the end of hour two								
Volume *	0.90	0.99	4.51	5.04	5.37	3.35	3.05	3.02
Free Acid †	0.047	0.070	0.325	0.499	0.432	0.423	0.296	0.252
Total Acid †	0.051	0.073	0.365	0.537	0.464	0.445	0.323	0.276
Dogs fasting throughout								
Volume *	1.24	3.14	4.66	4.99	3.64	2.90	1.71	2.82
Free Acid †	0.083	0.373	0.581	0.573	0.366	0.251	0.126	0.154
Total Acid †	0.094	0.400	0.619	0.615	0.404	0.283	0.141	0.186

\* Volume in ml.

† Acid in m.Eq./vol.



TABLE 5.--Mean Hourly Heidenhain Pouch Secretions in Awake Dogs

Group A (Proximal Enterectomy)

Hours	1	2	3	4	5	6	7	8	S.S. <sup>†</sup>
Dogs fed at the end of hour 2									
Volume <sup>*</sup>	1.00	1.90	5.01	4.15	4.41	2.67	2.91	2.41	N.S.
Free Acid <sup>†</sup>	0.092	0.158	0.305	0.367	0.329	0.238	0.168	0.162	N.S.
Total Acid <sup>†</sup>	0.096	0.166	0.343	0.403	0.353	0.263	0.194	0.186	N.S.
Dogs fasting throughout									
Volume <sup>*</sup>	1.66	1.99	2.34	2.35	1.90	1.71	1.84	2.48	p=0.05
Free Acid <sup>†</sup>	0.173	0.184	0.159	0.117	0.029	0.024	0.008	0.009	p=0.01
Total Acid <sup>†</sup>	0.178	0.198	0.175	0.129	0.040	0.036	0.020	0.018	p=0.01

\* Volume in ml.

† Acid in m.Eq./vol.

† Statistical significance of the volume and acid concentrations compared with the controls.





TABLE 6.--Mean Hourly Heidenhain Pouch Secretions in Awake Dogs

Group B (Distal Enterectomy)

Hours	1	2	3	4	5	6	7	8	S.S. <sup>‡</sup>
Dogs fed at the end of hour 2									
Volume <sup>*</sup>	3.56	6.61	11.00	8.65	4.87	3.74	1.74	1.79	N.S.
Free Acid <sup>†</sup>	0.394	0.754	1.201	1.256	0.624	0.371	0.131	0.147	N.S.
Total Acid <sup>†</sup>	0.414	0.795	1.275	1.316	0.691	0.404	0.156	0.186	N.S.
Dogs fasting throughout									
Volume <sup>*</sup>	1.67	1.92	1.86	2.29	2.41	1.37	1.83	1.35	p=0.05
Free Acid <sup>†</sup>	0.149	0.138	0.138	0.133	0.135	0.025	0.042	0.018	p=0.01
Total Acid <sup>†</sup>	0.164	0.157	0.155	0.149	0.156	0.035	0.081	0.031	p=0.05

<sup>\*</sup> Volume in ml.<sup>†</sup> Acid in m.Eq./vol.<sup>‡</sup> Statistical significance of the volume and acid concentrations compared with the controls.



The rise occurred a little later in Group B (during the fourth and fifth hour), than in the controls and Group A (during the third and fourth hour). Once again in Group B, the secretion during the final hour of collection was less than during the first hour, while in both controls and Group A, it remained greater.

In neither Group A nor B was a hypersecretion demonstrated in the fasting collections; on the contrary, both groups secreted substantially less than before their enterectomies. On the basis of this observation alone, it would appear that food is a necessary ingredient to stimulate gastric hypersecretion following enterectomy.

#### Eight Hour Anaesthetized Measurements

With the animals anaesthetized, a difference was noted between the two groups.

Group A secreted less than the controls, both in the fed and fasting state (Figures 10 and 12); the decrease in volume of gastric juice was small and not statistically significant (Tables 7, 8, and 9), but there was an important decrease in its acidity ( $p = 0.05$ ), (Tables 19 and 21).

Group B, on the other hand, produced an increased secretion over the controls (Tables 8 and 10). In the fed state, both volume and acid were significantly increased ( $p = 0.05$ ) (Table 20), (Figure 10 and 11), while in the fasting state, the increments were smaller and not statistically significant (Figures 12 and 13) (Table 22).

In the fasting state, the diurnal rise in Heidenhain Pouch secretion was seen to occur earlier (second and third hours) than when the dogs were awake (third and fourth hours).



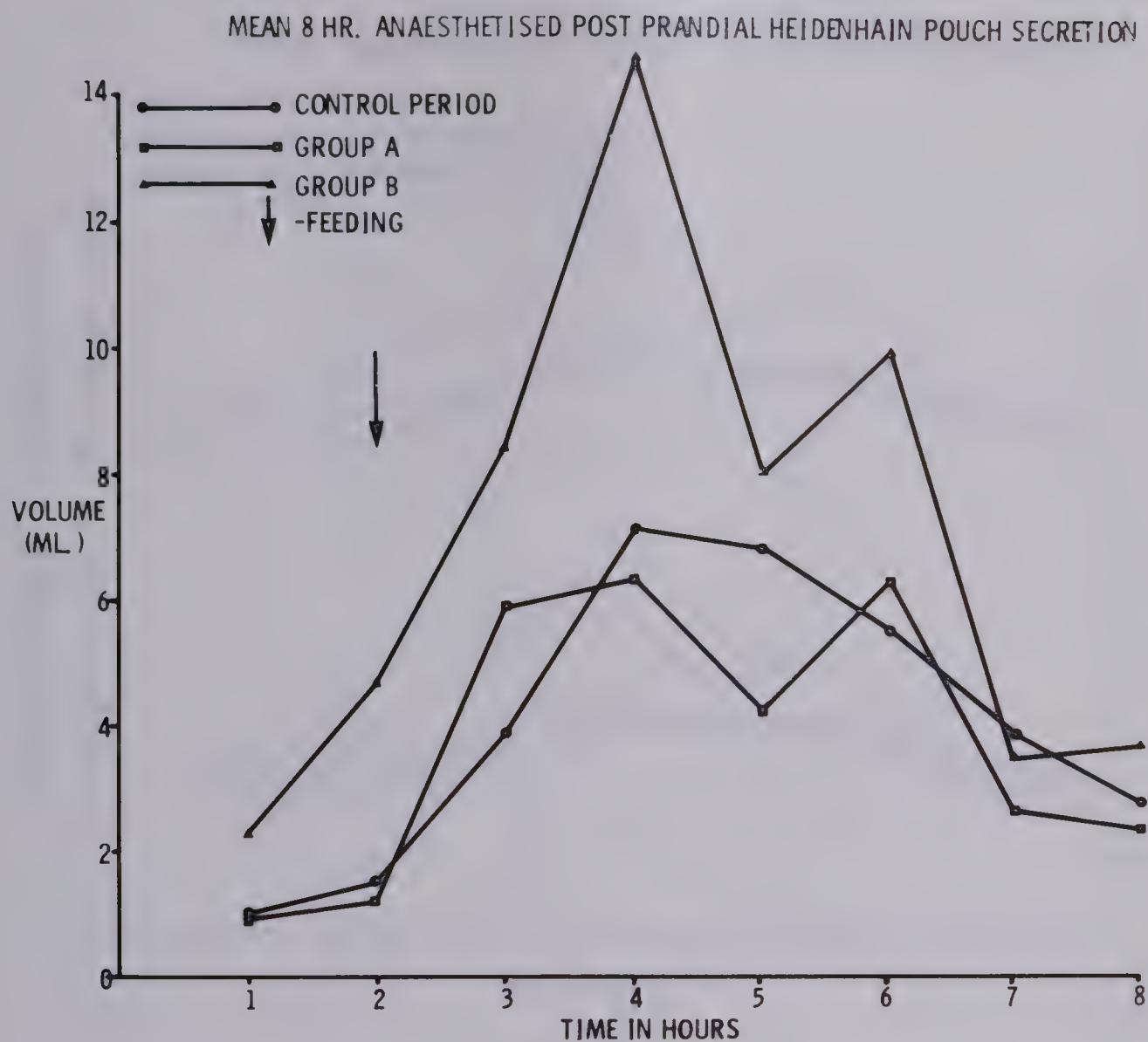


Fig. 10.--Comparison of the mean hourly anaesthetized post-prandial Heidenhain Pouch secretory volumes of control dogs, Group A and Group B dogs. Enterectomy had no significant effect on that of Group A, but significantly increased that of Group B ( $p = 0.05$ ).





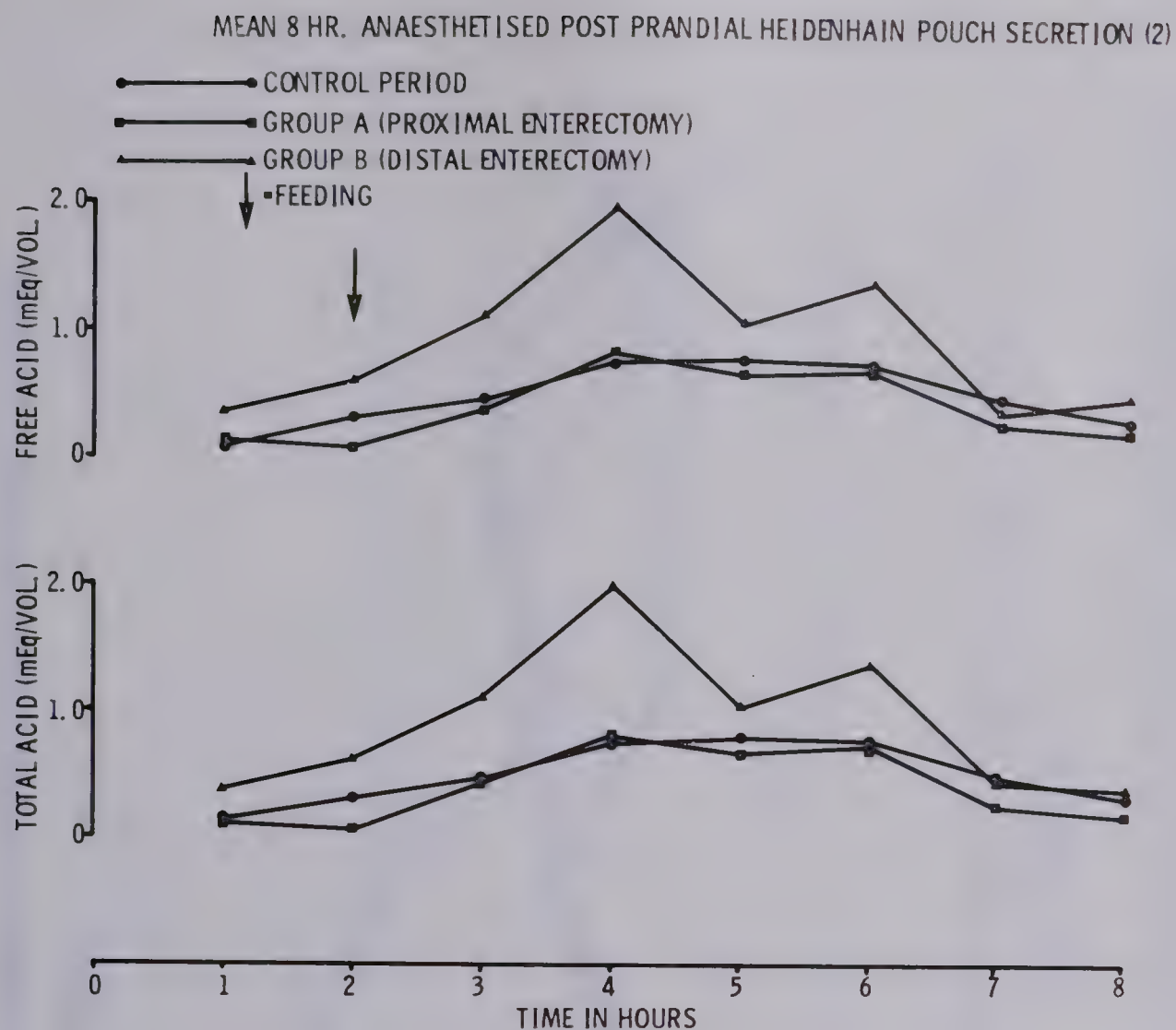


Fig. 11.--Comparison of the mean hourly anaesthetized post-prandial Heidenhain Pouch acid concentrations of control dogs, Group A and Group B dogs. Enterectomy significantly decreased the free and total acid concentration in Group A ( $p = 0.05$ ), and significantly increased the free and total acid in Group B ( $p = 0.05$ )



# MEAN 8 HR. ANAESTHETISED FASTING HEIDENHAIN POUCH SECRETION

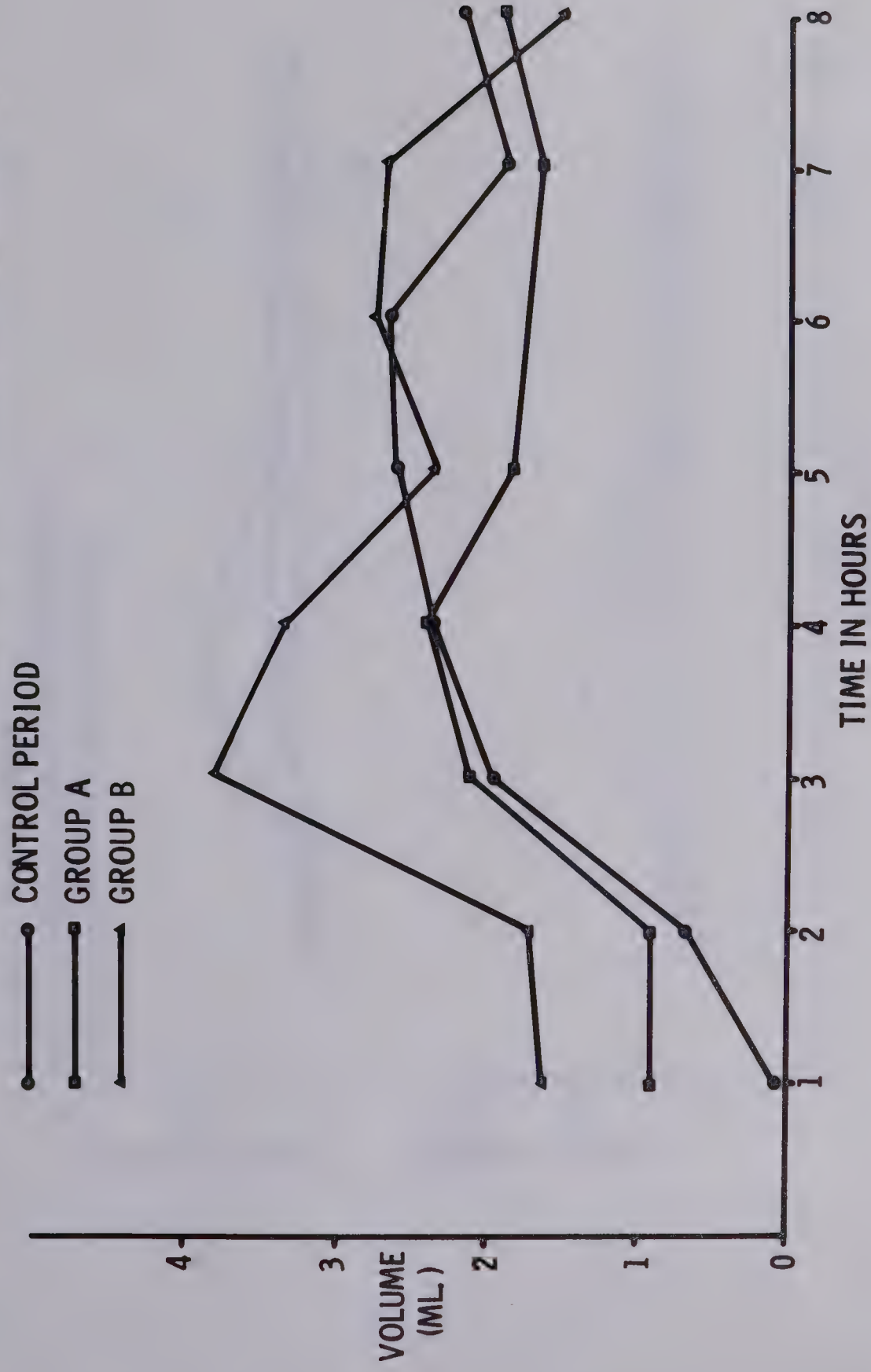


Fig. 12.--Comparison of the mean hourly anaesthetized fasting Heidenhain Pouch secretory volumes of control dogs, Group A and Group B dogs. No significant changes occurred following enterectomy.



# MEAN 8 HR. ANAESTHETISED FASTING HEIDENHAIN POUCH SECRETIONS (2)

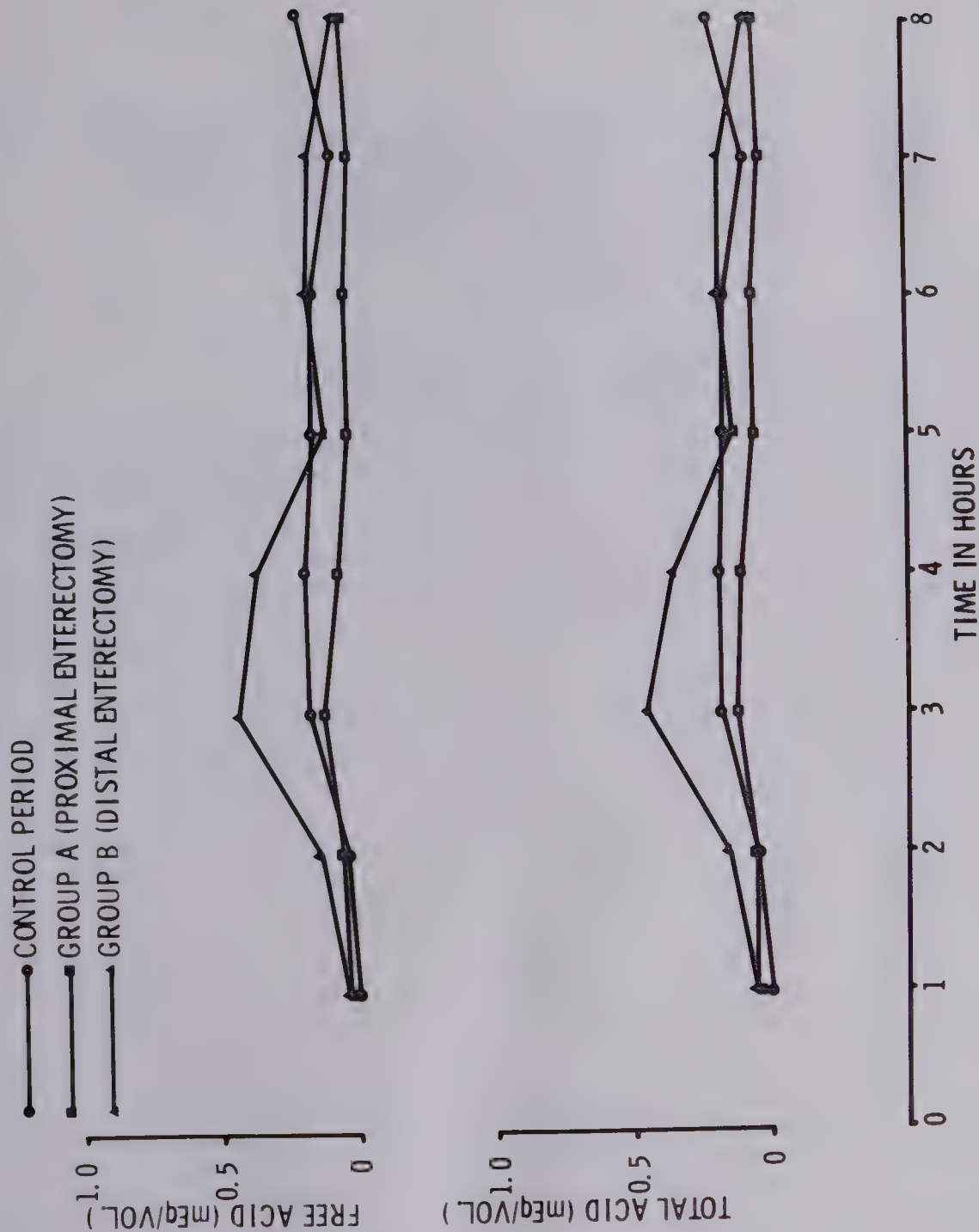


Fig. 13.--Comparison of the mean hourly anaesthetized fasting Heidenhain Pouch acid concentrations of control dogs, Group A, and Group B dogs. Enterectomy produced a significant fall in free and total acid concentration in Group A ( $p = 0.05$ ) but no significant change in Group B dogs.





TABLE 7.--Mean Total Eight Hourly Heidenhain Pouch Secretions in Anaesthetized Controls and Enterectomized Dogs, Postprandial and Fasting, and the Statistical Significance of the Changes Following Enterectomy

	Control	Group A	Group B
Postprandial volume <sup>*</sup>	32.62	30.12 (N.S.)	55.21 (p=0.05)
Fasting volume	14.40	13.58 (N.S.)	19.70 (N.S.)

<sup>\*</sup> Volume in ml.



TABLE 8.--Mean Hourly Heidenhain Pouch Secretions in Anaesthetized Dogs  
Controls

	Hours							
	1	2	3	4	5	6	7	8
Dogs fed at the end of hour two								
Volume *	1.03	1.55	3.91	7.18	6.86	5.53	3.85	2.72
Free Acid <sup>†</sup>	0.100	0.305	0.433	0.748	0.782	0.710	0.446	0.280
Total Acid <sup>†</sup>	0.124	0.326	0.461	0.797	0.800	0.763	0.474	0.303
Dogs fasting throughout								
Volume *	0.09	0.69	1.99	2.39	2.60	2.65	1.86	2.16
Free Acid <sup>†</sup>	0.000	0.042	0.176	0.186	0.156	0.156	0.082	0.200
Total Acid <sup>†</sup>	0.000	0.050	0.192	0.197	0.173	0.176	0.095	0.222

\* Volume in ml.

<sup>†</sup> Acid in m.Eq./vol.



TABLE 9.--Mean Hourly Heidenhain Pouch Secretions in Anaesthetized  
Dogs Group A (Proximal Enterectomy)

Hours	1	2	3	4	5	6	7	8	S.S. <sup>†</sup>
Dogs fed at the end of hour 2									
Volume <sup>*</sup>	0.99	1.24	5.91	6.38	4.29	6.29	2.64	2.38	N.S.
Free Acid <sup>†</sup>	0.110	0.079	0.388	0.797	0.645	0.676	0.244	0.176	p=0.05
Total Acid <sup>†</sup>	0.144	0.093	0.443	0.809	0.681	0.716	0.265	0.195	p=0.05
Dogs fasting throughout									
Volume <sup>*</sup>	0.92	0.94	2.14	2.40	1.86	1.76	1.65	1.91	N.S.
Free Acid <sup>†</sup>	0.045	0.058	0.128	0.068	0.033	0.048	0.017	0.038	p=0.05
Total Acid <sup>†</sup>	0.052	0.067	0.144	0.103	0.067	0.074	0.030	0.052	p=0.05

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of volume and acid concentrations compared with controls.





TABLE 10.--Mean Hourly Heidenhain Pouch Secretions in Anaesthetized  
Dogs Group B: (Distal Enterectomy)

Hours	1	2	3	4	5	6	7	8	S.S.†
Dogs fed at the end of hour 2									
Volume*	2.32	4.67	8.43	14.57	8.08	9.91	3.55	3.69	p=0.05
Free Acid†	0.383	0.598	1.099	1.943	1.001	1.348	0.433	0.390	p=0.05
Total Acid†	0.396	0.617	1.132	1.991	1.036	1.354	0.448	0.455	p=0.05
Dogs fasting throughout									
Volume*	1.64	1.73	3.80	3.33	2.32	2.72	2.66	1.50	N.S.
Free Acid†	0.044	0.139	0.436	0.351	0.118	0.178	0.156	0.079	N.S.
Total Acid†	0.052	0.154	0.456	0.372	0.145	0.194	0.175	0.083	N.S.

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of volume and acid concentrations compared with controls.



Eight hours anaesthetized fed secretions.-- The sum of the means in this category were; 33 ml. for the controls; 30 ml. for Group A; and 55 ml. for Group B (Table 10),

There is a similarity in the pattern of these secretions and that of the awake and fed animals. Group A secreted less than the control dogs, but Group B produced a significant acid hypersecretion ( $p = 0.05$ ) (Figures 10 and 11).

Eight hours anaesthetized fasting secretions.-- The sum of the means in this category were: 14 ml. for the controls; 14 ml. for Group A; and 20 ml. for Group B (Table 10).

The volume of Heidenhain Pouch secretion in this category was less than in any other, suggesting that either the anaesthetic exerts a depressor effect on gastric secretion, or that external stimuli apart from food may act to increase gastric secretion.

As in the majority of the eight hour secretions, Group A secreted less than the controls, while Group B hypersecreted. Neither change in volume was statistically significant, but the decreased acidity in Group A was significant ( $p = 0.05$ ).

## II. Second Stage

In the second stage of the experiment, the thoracic duct lymph was diverted in Group A and B dogs, and subsequently reinfused intravenously. Heidenhain Pouch secretions were measured hourly for eight hours. During the first two hours, baseline Heidenhain Pouch secretions from the anaesthetized and thoracotomized dogs were collected; over the next four hours, those from the fed animal with the thoracic duct lymph diverted were collected; and during the last two hours, the



hourly collections were from the dog while the diverted lymph was being reinfused into a systemic vein.

#### Group A

The mean baseline Heidenhain Pouch secretions for the anaesthetized and thoracotomized Group A dogs was lower than that for Group B, and no significant change occurred on diverting the thoracic duct lymph and feeding them. Although the Heidenhain Pouch secretions were minimal during this four hour postprandial period, it is interesting that virtually no acid was produced in it (Figures 14 and 15). Intravenous reinfusion of the lymph, however, produced a highly significant increase in their Heidenhain Pouch secretion in every case ( $p < 0.01$ ), (Figure 16), (Tables 23 and 25).

#### Group B

In Group B, the baseline Heidenhain Pouch secretion of the anaesthetized and thoracotomized dogs was approximately double that of Group A (Figure 14), but no significant change was produced either by feeding the dogs and diverting the lymph, nor by reinfusing the lymph intravenously (Figure 17), (Tables 24 and 26).

#### General

The anaesthetized dogs with a thoracotomy secreted less from their Heidenhain Pouches than those with closed chests. The baselines are therefore lower in this category.

The expected rise in Heidenhain Pouch secretion after feeding the dogs did not occur in Group A, and was seen only rudimentarily in





MEAN 8 HR. ANAESTHETISED POST PRANDIAL HEIDENHAIN POUCH SECRETION BEFORE & AFTER T. D. DIVERSION

GROUP A (PROXIMAL ENTERECTOMY)

GROUP B (DISTAL ENTERECTOMY)

↓ - FEEDING, THORACIC DUCT DIVERTED

↓ - LYMPH REINFUSED I. V.

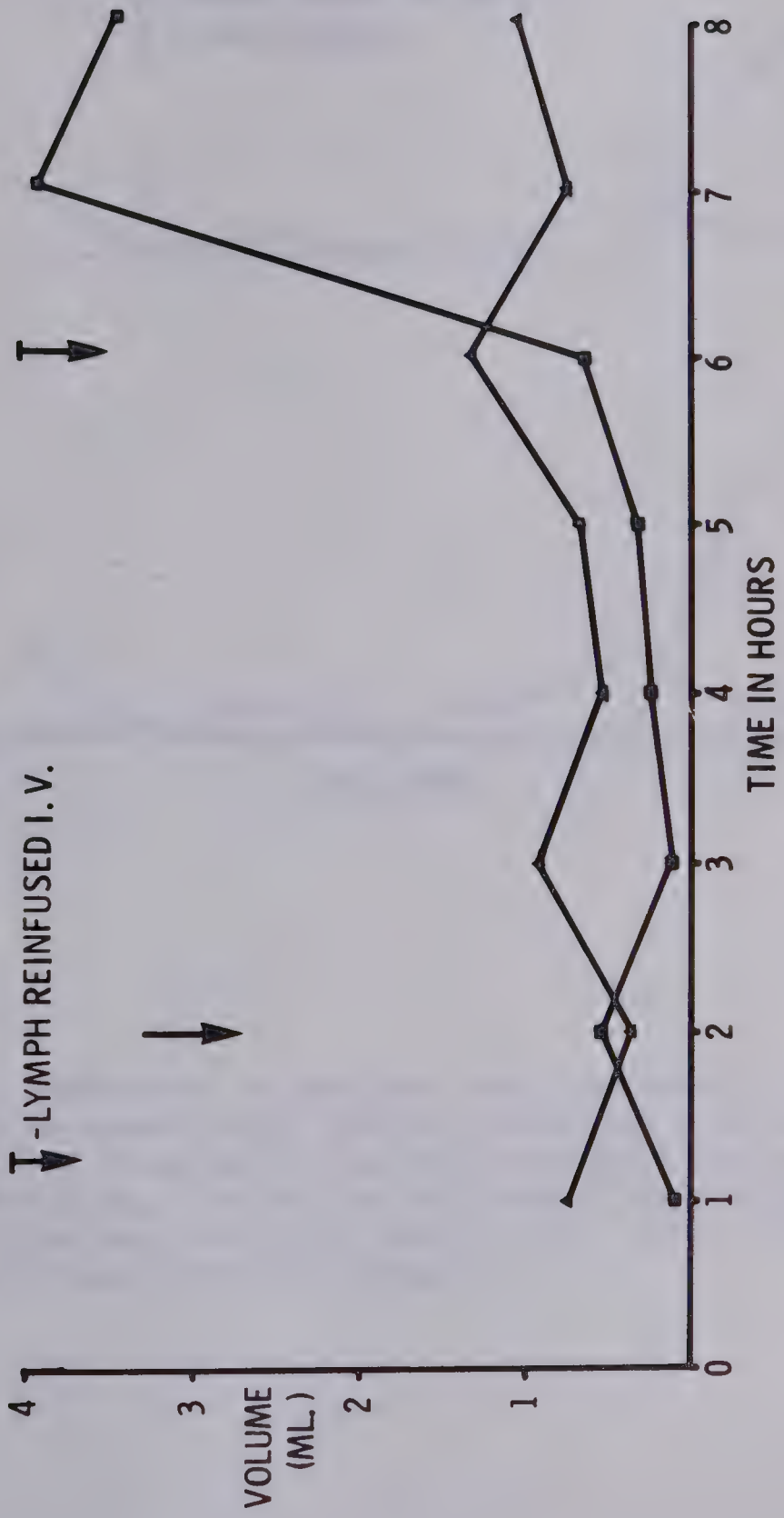


Fig. 14.--Comparison of the mean hourly Heidenhain Pouch secretory volumes of anaesthetized and thoracotomized Group A and B dogs. Feeding and diversion of the thoracic duct lymph had no measurable effect on either group. Reinfusion of diverted lymph significantly increased the secretory volume ( $p = 0.01$ ) of Group A dogs, but had no significant effect on that of Group B dogs.



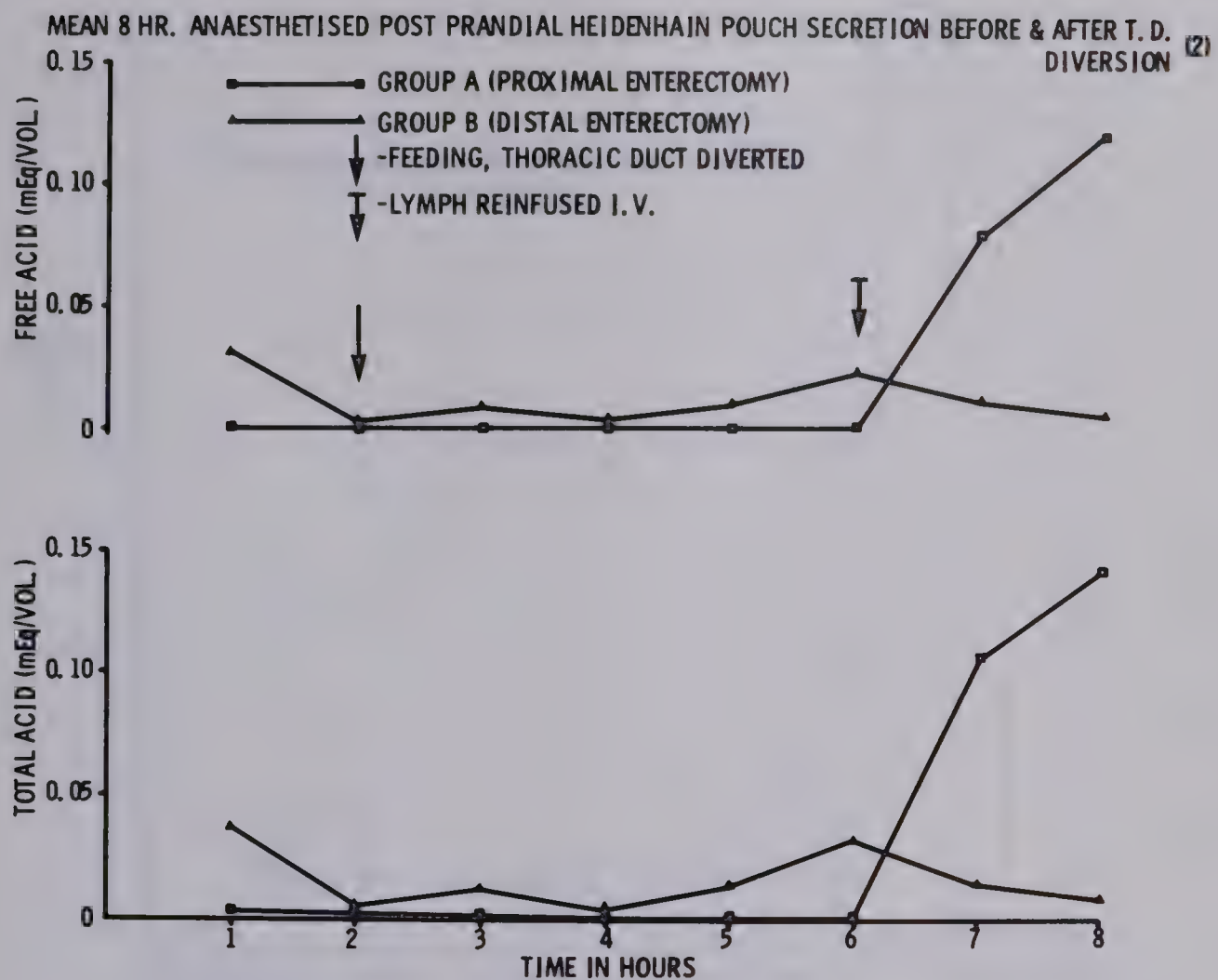


Fig. 15.--Comparison of the mean hourly Heidenhain Pouch acid concentrations in anaesthetized and thoracotomized Group A and B dogs. Feeding and diversion of thoracic duct lymph had no measurable effect in either group. Reinfusion of diverted lymph significantly increased the free and total acid concentration ( $p = 0.01$ ) in Group A, but had no significant effect in Group B.



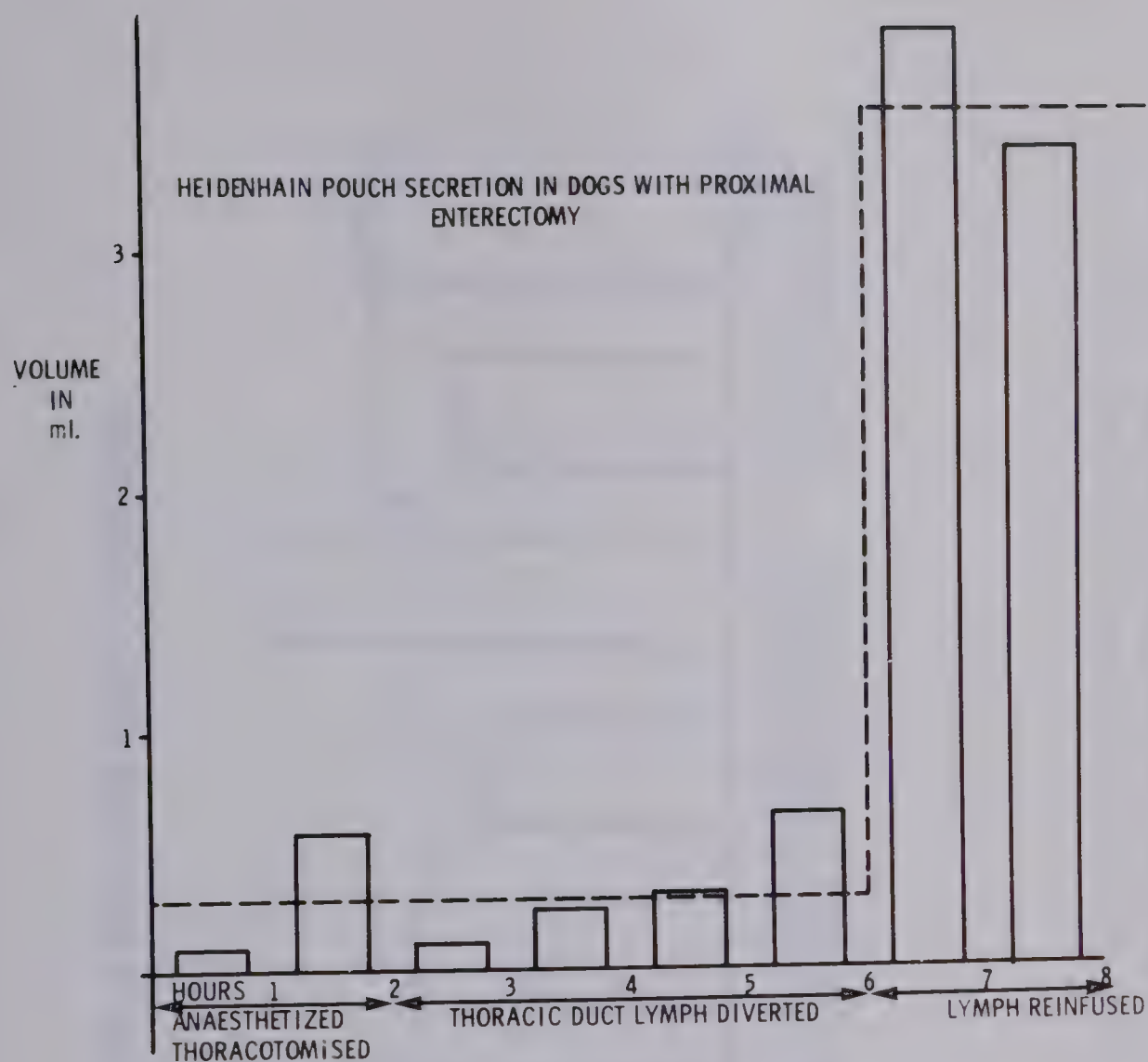


Fig. 16.--Hourly Heidenhain Pouch secretory volumes in anaesthetized and thoracotomized Group A dogs. Mean volumes for the two hour fasting, four hour postprandial lymph diverted, and two hour lymph reinfusion periods are illustrated with a dotted line.



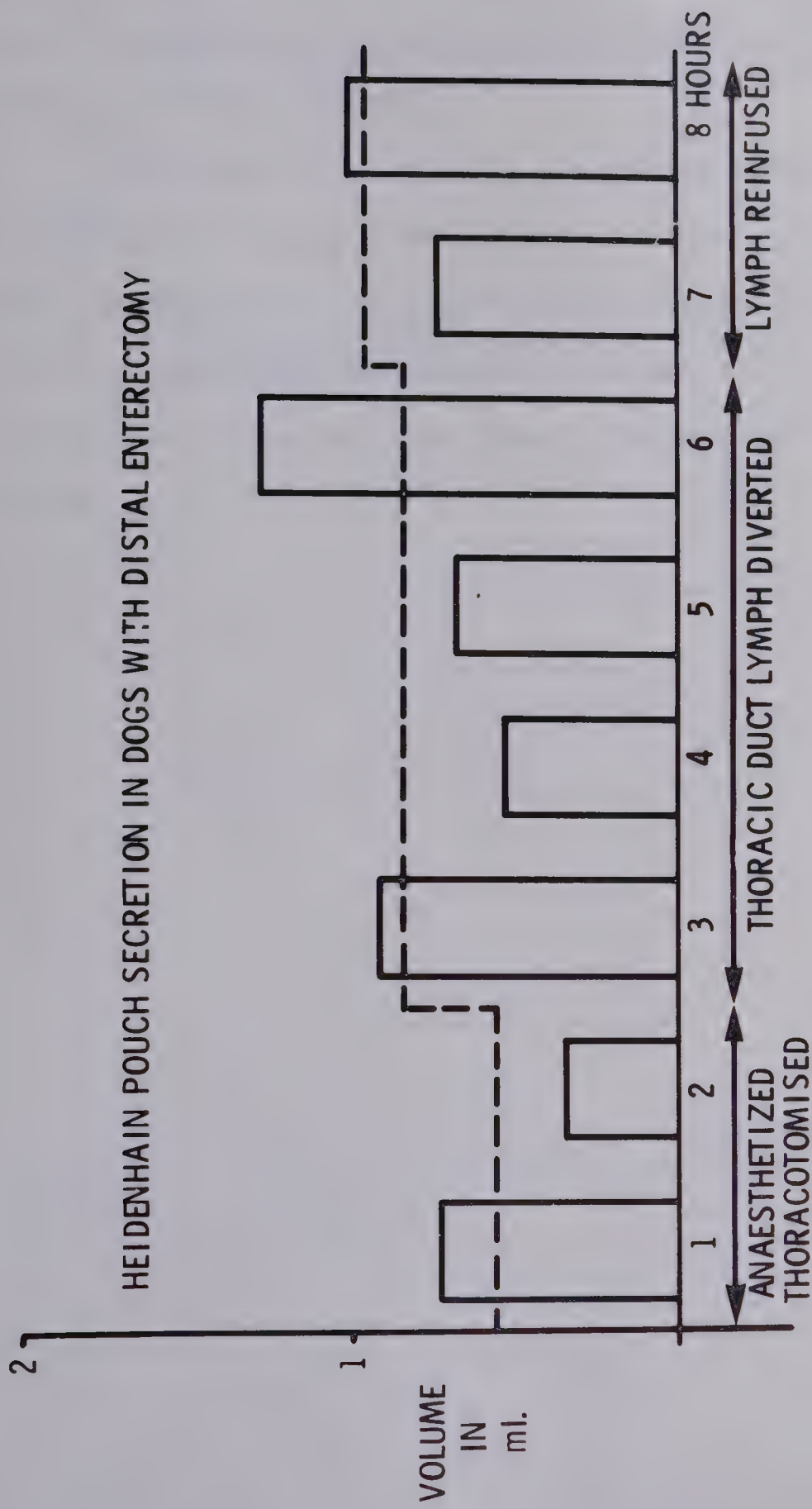


Fig. 17.--Hourly Heidenhain Pouch secretory volumes in anaesthetized and thoracotomized Group B dogs. Mean volumes for the two hour fasting, four hour postprandial lymph diverted and two hour lymph reinfusion periods are illustrated with a dotted line.





Group B. This phenomenon, and the simultaneous diversion of the thoracic duct lymph, are illustrated schematically in Figure 18. There was no significant difference in the amount of thoracic duct lymph collected from both groups.

There was a statistically significant difference ( $p = 0.05$ ) between the Heidenhain Pouch secretions in Groups A and B during the first six hours of collection, when those of Group B were greater, and a similar statistical difference between the two groups during the last two hours of collection, when those of Group A were greater (Tables 27 and 28).



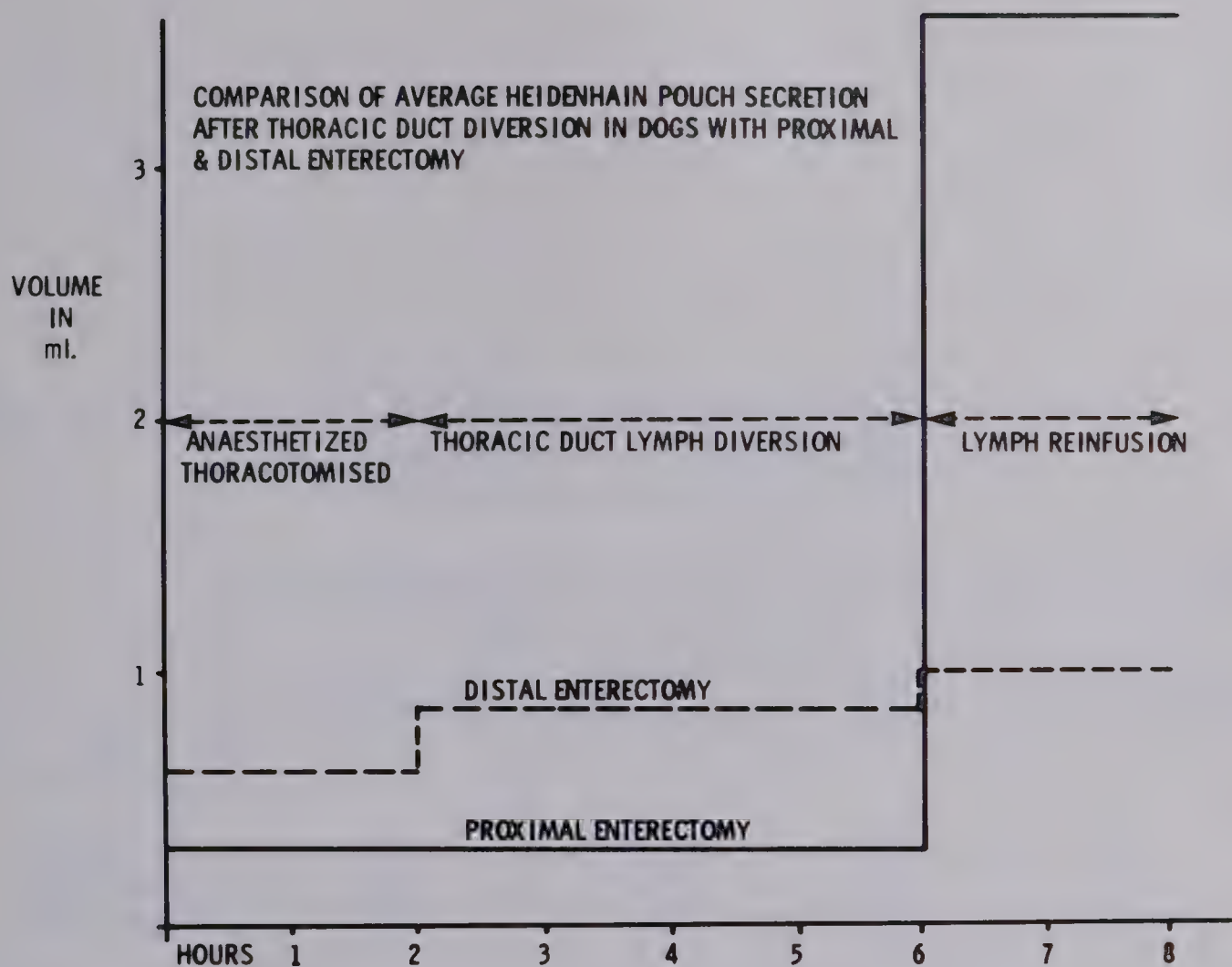


Fig. 18.--Comparison of mean Heidenhain Pouch secretory volumes in anaesthetized and thoracotomized Group A and B dogs for the two hour fasting, four hour postprandial lymph diverted, and two hour lymph reinfusion periods.



TABLE 11.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

	Proximal Enterectomy			
	% Difference	Standard deviation	P value	Significance
24 hours fed				
Volume	1.49	36.554	2.249	5 %
Free Acid	1.69	5.762	2.146	5 %
Total Acid	1.55	5.857	2.073	5 %





TABLE 12.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

Distal Enterectomy				
	% Difference	Standard deviation	P value	Significance
24 hours fed				
Volume	1.41	33,438	2.206	5 %
Free Acid	1.44	5.374	1.805	N.S.
Total Acid	1.32	5.502	1,728	N.S.



TABLE 13.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

Proximal Enterectomy				
	% Difference	Standard deviation	P value	Significance
24 hours not fed				
Volume	1.85	30.517	1.626	N.S.
Free Acid	3.42	4.383	1.84	N.S.
Total Acid	3.36	4.747	1.836	N.S.



TABLE 14.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

Distal Enterectomy				
	% Difference	Standard deviation	P value	Significance
24 hours not fed				
Volume	0.04	19,906	0.038	N.S.
Free Acid	2.39	3,087	1.451	N.S.
Total Acid	2.33	3.168	1,516	N.S.



TABLE 15.--Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures

Proximal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours awake fed				
Volume	6.96	0.683	0.914	N.S.
Free Acid	25.15	0.094	1.962	N.S.
Total Acid	23.28	0.096	1.942	N.S.





TABLE 16.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

Distal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours awake fed				
Volume	46.16	3.085	1.804	N.S.
Free Acid	70.21	0.414	2.163	N.S.
Total Acid	67.91	0.43	2.141	N.S.



TABLE 17.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

Proximal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours awake not fed				
Volume	42.74	1.113	2.808	5 %
Free Acid	112.38	0.178	3.578	1 %
Total Acid	110.23	0.187	3.693	1 %



TABLE 18.--Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures

Distal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours awake not fed				
Volume	52.27	1.155	3.185	5 %
Free Acid	105.23	0.171	3.57	1 %
Total Acid	98.86	0.184	3.491	5 %





TABLE 19.--Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures

Proximal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours asleep fed				
Volume	7.99	1.347	0.658	N.S.
Free Acid	19.47	0.101	2.365	5 %
Total Acid	20.29	0.09	2.917	5 %



TABLE 20.--Statistical Analysis Comparing Mean Heidenhain Pouch  
Secretions Under the Various Conditions of  
Collection with Control Figures

Distal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours asleep fed				
Volume	51.44	2.516	3.175	5 %
Free Acid	62.51	0.384	3.186	5 %
Total Acid	58.1	0.391	2.995	5 %



TABLE 21.--Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures

Proximal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours asleep not fed				
Volume	5.92	0.552	0.531	N.S.
Free Acid	79.03	0.072	2.787	5 %
Total Acid	61.08	0.071	2.563	5 %



TABLE 22.--Statistical Analysis Comparing Mean Heidenhain Pouch Secretions Under the Various Conditions of Collection with Control Figures

Distal Enterectomy				
	% Difference	Standard deviation	P value	Significance
8 hours asleep not fed				
Volume	30.95	0.876	2.131	N.S.
Free Acid	40.12	0.117	1.511	N.S.
Total Acid	38.36	0.123	1.505	N.S.





TABLE 23.--Hourly Heidenhain Pouch Secretion in Group A Dogs During Baseline Collections (Hours One and Two), Postprandial Collections with Thoracic Duct Lymph Diverted (Hours Three, Four, Five and Six), and Post Lymph. Reinfusion Collections (Hours Seven and Eight); and Mean Hourly Volumes and Acid Concentrations

	Hours							
	1	2	3	4	5	6	7	8
Number of Dog								
F 622	0	0	0	0	0	0	2.5	3.0
F 307	0	0	0	0	0	2.5	11.0	10.0
F 678	0.3	0.1	0.1	0.1	0	0	2.5	1.0
F 740	0.1	0.3	0	0	0	0	3.0	2.0
F 1232	0.1	1.5	0.1	0	0.4	0.3	3.0	2.5
F 564	0.1	1.5	0.6	1.5	1.5	1.1	1.4	2.0
Means								
Volume *	0.1	0.6	0.1	0.3	0.3	0.6	3.9	3.4
Free Acid †	0.000	0.000	0.000	0.000	0.000	0.000	0.078	0.120
Total Acid †	0.002	0.002	0.001	0.000	0.000	0.000	0.105	0.141

\* Volume in ml.

† Acid in m.Eq./vol.



TABLE 24.--Individual Hourly Heidenhain Pouch Secretion in Group B Dogs During Baseline Collections (Hours One and Two), Postprandial Collections with Thoracic Duct Lymph Diverted (Hours Three, Four, Five, and Six), and Post Lymph. Reinfusion Collections (Hours Seven and Eight); and Mean Hourly Volumes and Acid Concentrations

	Hours							
	1	2	3	4	5	6	7	8
Number of Dog								
F 303	0	0	0.2	0	0.3	0.2	0.4	0.5
F 306	2	0.1	0	0.1	0.6	1.0	0.8	0.7
F 357	2	0.1	0.2	0.3	0.1	3	0.1	0.1
F 335	0.1	1.5	1.2	1.2	1	2	1.4	2.0
F 550	0.3	0.4	3.5	1.2	2	1.4	1.5	2.0
F 1040	0	0.1	0.4	0.4	0.1	0.3	0.3	0.8
Means								
Volume <sup>*</sup>	0.7	0.4	0.9	0.6	0.7	1.3	0.8	1.0
Free Acid <sup>†</sup>	0.032	0.002	0.008	0.003	0.010	0.025	0.010	0.005
Total Acid <sup>†</sup>	0.037	0.003	0.012	0.004	0.013	0.032	0.013	0.007

\* Volume in ml.

† Acid in m.Eq./vol.



TABLE 25.--Comparison of Hours Seven and Eight with the First Six Hours  
of Secretion in the Thoracic Duct Diversion in  
Proximal Enterectomy

	% Difference	Standard deviation	P value	Significance
Volume	35.5	0.245	13.576	1 %
Free Acid	50	0.014	7.14	1 %
Total Acid	48.67	0.012	10.348	1 %





TABLE 26.--Comparison of Hours Seven and Eight with the First Six Hours  
of Secretion in the Thoracic Duct Diversion in  
Distal Enterectomy

	% Difference	Standard deviation	P value	Significance
Volume	2	0.286	0.442	N.S.
Free Acid	6.14	0.01	0.577	N.S.
Total Acid	5.62	0.012	0.577	N.S.



TABLE 27.--Mean of the First Six Hours of the Thoracic Duct Diversion  
in Dogs with Distal Enterectomy Compared with the Mean  
of the First Six Hours of Duct Diversion in Dogs  
with Proximal Enterectomy

	% Difference	Standard deviation	P value	Significance
Volume	76.3	0.363	2.82	5 %
Free Acid	200	0.012	2,677	5 %
Total Acid	181.07	0.014	2,767	5 %



TABLE 28.--Mean of the Last Two Hours of the Thoracic Duct Diversion  
in Dogs with Distal Enterectomy Compared to the Last  
Two Hours of the Proximal Duct Diversion

	% Difference	Standard deviation	P value	Significance
Volume	30.55	0.39	7.109	5 %
Free Acid	42.97	0.03	3.089	N.S.
Total Acid	42.48	0.025	4.444	5 %



## DISCUSSION

### I. Twenty-Four Hour Studies

The gastric hypersecretion that follows massive enterectomy was demonstrated in both Group A and Group B dogs, during the twenty-four hour postprandial collections, when significant increases over the control secretions were noted. This hypersecretion may be the result either of adding a secretagogue, or removing an inhibitor to gastric secretion, or both.

In the twenty-four hour fasting collections, the hypersecretion was present in Group A dogs, but not in those of Group B. Since both Groups hypersecreted when fed, it is possible that the hypersecretory potential remains present in both groups when fasting, but in the case of distally enterectomized dogs, requires the additional stimulus of intraluminal food to show it.

### II. Eight Hour Studies

The modest decrease in Heidenhain Pouch secretion after fifty-five per cent proximal enterectomy in awake and anaesthetized, fed and fasting dogs has not been described before, to the best of the author's knowledge. It suggests that either a weak secretagogue was removed with the jejunum, or that the influence of an inhibitor to gastric secretion is being more strongly felt in the absence of the proximal half of the small intestine.





The increased Heidenhain Pouch secretion that occurred in Group B dogs in the eight hours awake fed, and eight hours anaesthetized fed and fasting categories, may indicate the existence of an ileal inhibitor to gastric secretion, or of a jejunal secretagogue. The effect of distal enterectomy would be to remove this inhibitor, or permit the jejunal secretagogue to act more effectively. The failure of the mean eight hour awake fasting samples to show a hypersecretion may be further evidence that a food stimulus is needed in awake and fasting dogs with a distal enterectomy. A small rise in Heidenhain Pouch secretion was seen in distally enterectomized fasting dogs, but only under anaesthetized conditions.

Gastric hypersecretion following enterectomy is an established response that has received much attention, and is demonstrated in our work in the postprandial eight hour studies on Group B dogs. In the Group A (proximally resected) dogs, a gastric hyposecretion was observed. This is a phenomenon that has not so far been demonstrated. In order to produce a decreased Heidenhain Pouch secretion, the effect of known secretagogues such as antral gastrin would have to be overcome. This argues in favour of an ileal inhibitor.

On the other hand, convincing evidence of a secretagogue comes from the studies on diversion and reinfusion of thoracic duct lymph. With the thoracic duct intact, all anaesthetized dogs who were fed showed a steep rise in Heidenhain Pouch secretion within the hour. But the dogs that were fed, and whose thoracic duct lymph simultaneously diverted, showed no detectable change in Heidenhain Pouch secretion for the four



hours that followed. On reinfusion of the lymph at the end of this period, the highly significant rise in Heidenhain Pouch secretion that occurred in Group A dogs furnishes good evidence of the presence of a lymph borne humoral secretagogue in dogs with a proximal enterectomy.

Since the time of Pavlov, the ability of the small intestine to exert both stimulatory and inhibitory influence on gastric secretion has been recognized; but its contribution has been traditionally regarded as the least important "phase". As a result of recent post-enterectomy studies, the intestinal mechanism is assuming an unsuspected significance, and its role in the regulation of gastric secretion is undergoing reappraisal. An increase in gastric secretion has been shown to be mediated by the intestinal mechanism; the possibility exists that with a fuller understanding of the nature of this phenomenon, a decreased gastric acidity may be clinically achievable, with its consequent therapeutic application.

In addition to our above theories other possible mechanisms of gastric hypersecretion following enterectomy are discussed.

### III. Possible Mechanisms of Gastric Hypersecretion Following Enterectomy

#### Potential of Secretagogues

Prolonged gastric emptying time.-- Gastrin is secreted in proportion to the length of time that the antrum is stimulated (1). Some authors have reported delayed gastric emptying times following enterectomy (2), while others have questioned it (3, 4, 5). Delayed gastric emptying was not a feature of Chow's dogs postenterectomy (5), the barium mixture transit time remaining at three hours both before and after the resections.



Liver damage.-- It has been postulated that damage to the liver in the course of surgery for enterectomy had resulted in an inability to inactivate secretagogues such as histamine(6). Chow (5) detected no histological nor biochemical change in canine livers after massive enterectomy, and pointed out that the hypersecretions he produced were immediate, whereas hepatic cellular degeneration would be a slower, biological process.

Infection.-- Sepsis has been shown to cause a rise in gastric acid production (7), but was not a feature of the postoperative course of Chow's animals.

Corticosteroids.-- The adrenocortical response to stress in man has been shown to produce a transient gastric hypersecretion (8). The stress following a surgical procedure like enterectomy is short lived in the dog, but protagonists (9) and antagonists (4) of this view as a source of the gastric hypersecretion following enterectomy may be quoted. Chow (5) found that the Heidenhain Pouch secretions were unchanged after a sham operation in which he transected the bowel and re-sutured it without resection; and concluded that this was not the mechanism of hypersecretion.

"Intestinal Phase".-- In the Pavlovian concept, this phase occupied the least important position of the three mechanisms. It has, however, assumed a new importance after enterectomy, and is the subject of this study.

Traditionally, antral gastrin is implicated in the production of acid from the parietal cells, whether by the direct action of the





gastric "phase", or the indirect "permissive" action of the vagal "phase". Chow (5) has produced a substantial acid hypersecretion in the absence of the antrum, by performing a massive enterectomy on antrectomized dogs. This may be evidence of a secretagogue from the retained intestine acting on a target organ other than the pyloric antrum. A gastrin like material has been extracted from the duodenum of hogs (10), and it is possible that similar hormones may be present throughout the small intestine. The proposed secretagogue may be a weak stimulator of gastric secretion, or it may act to potentiate gastrin.

Evidence in favour of this mechanism comes from the studies of Yakimets and Bondar (11), and later Chow (5), from experiments in thoracic duct lymph diversion. Enterectomized, hypersecreting dogs sustained a fall in Heidenhain Pouch secretion when the thoracic duct lymph was diverted to the exterior, but resumed their hypersecretion when the lymph was reinfused intravenously. When the same procedure was performed on enterectomized and antrectomized hypersecreting dogs, the drop in secretion occurred on diverting the thoracic duct lymph, but there was no resumption of hypersecretion on lymph reinfusion.

#### Removal of Inhibitors

Increase in gastric secretion is now an established clinical phenomenon following massive enterectomy, although the mechanism remains obscure. If it were due entirely to the gain of a gastric secretagogue, it would not be possible to produce a decreased gastric secretion by removing any portion of the small intestine. In the dogs of Group A in the present experiment, a decreased Heidenhain Pouch



secretion was produced in every case in the eight hour collections.

Secretogogues such as antral gastrin continue to act in the experimental dogs. Reinforcement of their action by the gain of other secretogogues, strong or weak, following enterectomy might produce moderate to high levels of gastric juice production. But the repeated production of a decreased secretion (in the eight hour collections) against the known stimuli to gastric secretion, suggests a potent inhibitor rather than experimental artifact.

Inhibitors of gastric secretion derived from the antrum have been demonstrated by Menguy (12) and Harrison (13), and Thompson (14), have suggested the existence of a chalone. Secretin and Cholecystokinin (15, 16, and 17) are both known to exert an inhibitory influence on gastric secretion. Bile salts given intravenously have been shown to have a similar depressant action (18). In both groups of dogs in the present study, the enterectomies left antrum and duodenum intact, so that the known inhibitors described above were constant for both groups.

Other substances have been described which are thought to originate in the small intestine, and cause an inhibition of gastric secretion. Enterogastrone, described in 1930 by Kosaka and Lim (19), was thought to be liberated from the upper intestine in the presence of fat. Subsequently doubted by Gregory (20), the existence of this hormone in the substance of the small intestine may be germane to this study. It would, however, be necessary to postulate that it acted from the distal rather than the proximal small intestine; and the possibility arises that a related hormone, or an enterogastrone potentiator, may be implicated.



A chalone originating in the ileum, corresponding to enterogastrone in the jejunum, would furnish a partial explanation of the phenomena observed in this study.

Serotonin has been described as occurring along the whole length of the small intestine (21), and its effect on gastric secretion is known to be inhibitory (22, 23). Doubt persists as to the exact function of Serotonin in the alimentary tract, although intraperitoneal injection of it into rats has led to intense vasospasm and eventual ulceration (24). This has suggested a possible mode of action for the observations by Black (22), and Shay (23), of its inhibitory role in both secretion and motility of the digestive tract. Substances shown to release Serotonin from the wall of the small intestine after being introduced into the lumen include acid and hypertonic solution (25, 26, 27). It is possible that after a proximal enterectomy, the relatively undigested chyme entering the ileum would be both more acid, and more hypertonic than the customary physiological content, and that the Serotonin thus released might account for the decreased Heidenhain Pouch secretion observed in this study.

Histaminase, like Histamine, is also widely distributed along the length of the small intestine (28). Histamine is a potent stimulator of gastric secretion, and it follows that the enzyme antagonizes this effect. Grossman has demonstrated this action (29), and Sircus has used a Histaminase inhibitor to allow Histamine to work unopposed (30). Chow has proposed that after massive small intestinal resection, the secretory surface for Histaminase is sufficiently diminished to allow the cir-





culating Histamine to exert its full effect on the parietal cells, thus producing a gastric hypersecretion. He concedes that no physiological role has been established for this enzyme, and cites the work of Blair (31), who showed that antihistaminic drugs given systemically have no effect on parietal cell output.

The present study was designed to contrast the effects of proximal with distal enterectomy, and to determine whether any differences existed. Chow's study had been carried out on dogs with a "massive" enterectomy, or dogs with both a proximal and distal resection. Would a smaller resection have been sufficient to cause it? Was the simultaneous removal of both proximal and distal intestine synergistic or antagonistic? Was there a balance of secretagogue and inhibitor throughout the small intestine, responsible for the "intestinal phase"?

Chow's initial fall in Heidenhain Pouch secretion in both groups (i.e. enterectomized; and enterectomized and antrectomized) established the presence of a secretagogue carried in thoracic duct lymph. The absence of a return of hypersecretion in the second group on reinfusion of the lymph indicated that the secretagogue acted to stimulate or potentiate the events set in motion by the antral gastrin. In the present study, dogs having a proximal enterectomy hypersecreted on reinfusion of the lymph, but those with a distal resection did not. In both of these groups, the antra were intact, suggesting a difference in secretagogue production between proximal and distal intestine, and rendering a significant contribution from the colon unlikely.





A shorter length of intestine was resected in the present study than in that of Chow, but a greater hypersecretion was produced. However, the baseline levels in the enterectomized and thoracotomized dogs was low. No steep fall was therefore demonstrable on diverting the thoracic duct lymph of the present dogs, the baseline levels being already minimal. On reinfusion of the lymph, however, those dogs that hypersecreted (Group A) reached secretory levels seven times greater than their resting level, while Group B exhibited no measurable change. Thus, dogs in whom the ileum remains intact after a partial enterectomy have a potent stimulus to gastric secretion carried in the thoracic duct lymph. Removal of the ileum, and sparing of the jejunum, removes this stimulus.

When the thoracic duct is left intact, the opposite result is obtained from the two groups of enterectomized animals. The stimulus to hypersecrete when fed occurs in dogs from whom the ileum has been removed. This observation is in keeping with the data of Osborne in 1966 (4). It follows, therefore, that a minimum of two mechanisms, one stimulatory and the other inhibitory, must be acting to produce these conflicting results.

With the above idea in mind one simple explanation of the observed phenomena is that in addition to the antral secretagogue, a weak jejunal secretagogue and a stronger ileal inhibitor are present in the dogs intestinal tracts. This inhibitor may be labile, and quickly lose its potency outside the body, so that it is ineffective when reinfused intravenously with the lymph. The thoracic duct is proposed



as a transport for the jejunal secretagogue. Thus:

(i) When a proximal enterectomy is performed, the jejunal secretagogue is lost, and the resultant of the antral secretagogue and the strong ileal inhibitor is a small fall in Heidenhain Pouch secretion.

(ii) When a distal enterectomy is performed, the ileal inhibitor is lost, and the secretagogue(s) act together to raise the pouch secretion considerably.

(iii) When the thoracic duct lymph is diverted and reinfused in a proximally enterectomized dog, both the antral secretagogue and the ileal inhibitor are transported in the lymph, but the short lived inhibitor may be lost by the end of four hours, when the reinfusion takes place, and only the effect of the secretagogue is felt, giving the steep rise in Heidenhain Pouch secretion.

(iv) When the thoracic duct lymph is diverted in a distally enterectomized dog, the absence of the ileal inhibitor ensures a higher level of baseline Heidenhain Pouch secretion. On reinfusion of this lymph, the small rise in Heidenhain Pouch secretion over this relatively high baseline level represents the effect of the jejunal and antral secretagogues carried in this lymph.

#### IV. Conclusions

The Heidenhain Pouch hypersecretion that follows massive enterectomy may be produced mainly by resection of the distal small intestine.



Proximal enterectomy produces a mild decrease in Heidenhain Pouch secretion.

Reinfusion of thoracic duct lymph intravenously stimulates a twelvefold increase in Heidenhain Pouch secretion in dogs with a proximal enterectomy.

Reinfusion of thoracic duct lymph intravenously causes only a small rise in Heidenhain Pouch secretion in dogs with a distal enterectomy, but the baseline secretion is at a higher level.

The existence of a short lived ileal inhibitor to gastric secretion is proposed.





## FOOTNOTES

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PART 2. EFFECTS OF MASSIVE ENTERECTOMY AND AN ANTIPERISTALTIC SEGMENT  
ON GASTRIC SECRETION





## REVIEW OF THE LITERATURE ON REVERSED INTESTINAL SEGMENTS

In 1896, the Johns Hopkins Hospital Report published the results of an experiment conceived by Mall (1). He had reasoned that patients who had undergone massive small intestinal resection would derive benefit from reversal of the direction of peristalsis of a segment of the remaining bowel. William Halstead (2), his surgical colleague, tried the procedure on eleven dogs. Eight of these died within a few days from peritonitis, but the remaining three lived for eighteen, twenty-five, and sixty-four days respectively. It is recorded that the latter two had reversed segments measuring twenty-nine centimeters and eighty centimeters, and died of intestinal obstruction. As a result of this report, the procedure was condemned as lethal, and fell into disfavor. A quarter of a century was to pass before a scientific reappraisal of this original idea was undertaken.

In 1927, Ivy (3), using a variety of different lengths of reversed segment, was able to produce what he called a physiological partial obstruction in some dogs, and demonstrate that the principle was sound. Hammer (4, 5, 6) and his colleagues in Michigan subsequently carried out prolonged investigation in this field in the 1950's, and enunciated certain rules and criteria as a result of their study. They discovered that dogs with two-thirds of the small intestine resected can survive, but that diarrhea, cachexia and death within



ninety days follows removal of eighty per cent or more of the intestine. Reversal of about 5 cm. of the distal intestine was found to be effective in maintaining nutrition and keeping these dogs alive. Less successful results attended Hammer's more proximal reversals. The dogs in whom he reversed the entire duodenum following massive resection survived, the stomach and adjacent duodenum became dilated, and ulceration occurred at the proximal suture line after several months.

In 1959, Hammer and his associates (7) concluded that

"animals with 80 - 90% of the small bowel removed survive and maintain weight if 1 - 2 inches of the distal segment of remaining bowel is reversed, and reinserted into the intestine in an anti-peristaltic manner".

The site of these reversals was the distal ileum. Hammer noted at the same time that some human mesenteric thromboses involved 80 - 90% of the small intestine, and speculated on the therapeutic application of his finding to human patients.

The problem of whether reversed peristalsis would continue to act indefinitely against the stream was investigated by Singleton and Rowe in 1954 (8). Laparotomies were performed at varying intervals up to a year post-reversal, and peristalsis in the original direction was consistently observed in the reversed segment. This finding was corroborated in 1962 by Stahlgren et al (9), who recorded the maintenance of reversed peristalsis in dogs into whom they had inserted an anti-peristaltic segment of small intestine up to a year previously. In addition to this original observation, Singleton and Rowe noted that the stomach and intestine proximal to the site of the reversed segment became dilated, and that this dilatation sometimes extended into the reversed segment itself.



This dilatation was the result of the "physiological partial obstruction" that Ivy had described thirty years earlier. The length of the reversed segment determined the degree of obstruction, and the aim of the procedure was to achieve the longest antiperistaltic segment without producing a complete obstruction. Segments as small as 2.5 cm. had been shown not to alter metabolism in the dog. Sako (10) and his associates began experimenting with different lengths, and concluded that a reversed segment of 7.5 cm. in the jejunum was the optimum length in a small dog with a total intestinal length of about 300 cm. They found that weight was maintained in dogs with a massive enterectomy followed by this reversal, and stomach emptying and transit times were delayed for varying periods of time. Stahlgren (9) and his associates in 1962, had produced an obstruction in the small intestine of a dog by reversing a segment of jejunum five inches long, and subsequently relieved it by resecting one-half of the reversed segment.

Going one stage further, Mackby (11) discovered in 1965 that if the reversed segment was combined with a recirculating loop, the metabolism could be further increased in animals with an "optimum" recirculating loop. This procedure involved transposition of the entire residual segment of small intestine, but instead of a linear reversal, the bowel was fashioned into a recirculating loop with a circular motion of the contents, and the maximum length of linear antiperistaltic intestine (proximal to the loop) was only about 4 cm.--a length Mackby found to be optimal with a linear reversal. The distal portion of the loop was anastomosed to the remaining portion of the ileum, permitting





escape of the contents into the colon. Dogs with this arrangement have regained their preoperative weight and vigor, and produced semi-formed stools, while remaining in positive nutritional balance.

In 1965, there was general agreement that reversal of up to 7.5 cm. proximally, and up to 12 cm. distally, of small intestine, would often serve to compensate for severe loss of absorbing surface (12). But on occasion, anenteric cachexia would supervene even in dogs with this "optimal" reversal, and it became apparent that delay transit in some instances could not entirely compensate for massive loss of absorbing surface.

In 1965, Keller (13) began experimenting with paired reversed segments in dogs with a 90% enterectomy, and concluded that it was a superior procedure metabolically. In 1967, Fink and Olson (14) reported favorably on a patient to whom they had given two reversed segments to compensate for the "short bowel syndrome".

Much attention has been given to the optimum site for insertion of the reversed segment. Although Singleton (15) suggested in 1961 that a proximal enterectomy resulted in less steatorrhea and malnutrition than a distal enterectomy in dogs, subsequent metabolic and absorptive studies have shown the proximal small intestine to be the site of maximal absorption. In 1948, Cogswell (16) had demonstrated in dogs that inanition occurred more often after proximal than distal small intestinal resection. Borgstrom's (17) experiments in 1957 showed that the process of absorption of fat, carbohydrate and protein starts in the duodenum, and is complete after 100 cm. of jejunum. The conclusion



reached by Baldwin Price in 1965 (18) was that the proximal small intestine has a greater absorptive capacity than the distal, and that this capacity decreases from above downwards.

Unfortunately, the maximum length of reversed segment possible without causing obstruction increases from above downwards, as shown by Stahlgren in 1962 (9). He demonstrated in dogs that jejunal segments of no more than two inches could safely be reversed, while ileal segments of three to four inches were permissible. (This restriction refers only to reversal of small intestine, and not stomach. Poth (19) has shown that large antiperistaltic pouches of jejunum, fashioned in numerous different ways, may be used as gastric substitution pouches, and are compatible with ordinary alimentation and excellent nutrition).

Thus, the favored site for insertion of an antiperistaltic segment, if there were a choice, would be at a point about 90 cm. distal to the Ligament of Treitz, a conclusion arrived at independently by Madding (1965) (20), and Shepherd (1966) (21). "It would seem physiologically sound to delay the passage of food through this segment in which the concentration of enzymes is highest and absorption greatest" said Madding (20), referring to the first 90 cm. of jejunum.

The time available for absorption of intra-luminal contents will be proportional to the length of the intestine through which it passes. Although this time will be the same for all the intestinal contents, certain metabolic deficiencies are more keenly felt in the early stages post enterectomy. Thus, fat absorption has been shown to be more impaired than protein or carbohydrate absorption in patients with



"short bowel syndrome". Other early metabolic sequelae are deficiencies of Vitamins C, B<sub>12</sub>, and calcium, elements thought to be absorbed by the proximal small intestine. In addition to segmental reversal, supplementary supplies of these substances have been advocated (Althausen, 1949 (22); Singleton, 1961 (15)), and in the case of lack of fat absorption, oral medium-chain triglycerides have been shown to enhance weight gain and reduce the incidence of steatorrhea. (Winawer, 1966) (23).

Encouraging results from experimental work has resulted in clinical trials of reversed intestinal segments. Sixteen cases have been reported in the literature (24, 25, 26, 27). Six of these have been after resection for Crohn's disease, the most recent of these requiring the reversed segment to be removed, for a recurrence of the disease process, and another segment reversed. (Fink and Olson, 1967). Four have followed mesenteric infection, two have resulted from numerous resections for adhesions, and one, three resections in the gastrointestinal tract for recurrent carcinoma. Severe diarrhea has stimulated three reversals, the most recent of these being the post ileostomy diarrhea of a woman whose colon and distal ileum had been resected for ulcerative colitis. Her ileostomy output equalled 90% of her intake. Dramatic improvement followed reversal of a 10 cm. segment just proximal to the ileostomy, but after six months gradual relaxation of the segment has produced a return to the preoperative level, and the long term result appears poor.





## FOOTNOTES

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## METHODOLOGY

### I. General

Adult mongrel dogs of both sexes, weighing 13 - 25 kg. were used. Before being released to the laboratory, the animals had been kept at the Health Sciences Animal Center for two weeks for assessment of general condition. After receiving vaccination against canine hepatitis and distemper, deworming, and being passed as fit, they were brought to the Surgical-Medical Research Institute for the experiment. Their daily diet consisted of one can of commercial dog food daily,<sup>\*</sup> and unlimited water. Daily outdoor exercise was provided. Any dogs which became ill during the course of the experiment were excluded from the study.

### II. Experimental Plan

All six dogs were provided with a Heidenhain Pouch. Control body weights and Heidenhain Pouch secretions were recorded daily on these dogs for a month under various conditions and gastric emptying time was measured radiologically. After this a ninety per cent enterectomy was performed on all of them. Body weights, Heidenhain Pouch secretions, and gastric emptying times were again measured under identical conditions. Finally, an eight centimeter segment of jejunum was reversed, and reinserted into alimentary continuity in an anti-

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<sup>\*</sup>Dr. Ballard's





peristaltic direction, and further measurements made of body weight, Heidenhain Pouch secretion and gastric emptying times, under the same sets of conditions.

### III. Before Operation

Good general health was the criterion for surgery. Careful preoperative examination was carried out to ensure this, and the dog allowed to exercise up until the day of the surgery. Food was withheld for twenty-four hours before the procedure, and water for twelve hours.

### IV. Operation

In the preparation room, a superficial vein was displayed by shaving part of the leg, and anaesthesia induced by the intravenous administration of Nembutal, 30 mg./kg. body weight. A cuffed endotracheal tube was then inserted with a laryngoscope, under direct vision. The hair was removed from the abdominal skin with an electric razor, and the skin scrubbed with soap and warm water. The dog was then carried into the operating room, placed supine on the operating table with a leg tethered to each corner, and the operative site prepared with Betadine solution. Drapes were applied in the usual manner, strict sterile technique being maintained at all times. Care was taken to enter the abdomen through the linea alba, to facilitate a relatively bloodless entry, the incision being made from xiphisternum to umbilicus for Heidenhain Pouch construction, and more caudally for operations on the small intestine.



## V. Heidenhain Pouch Construction (Figure 1)

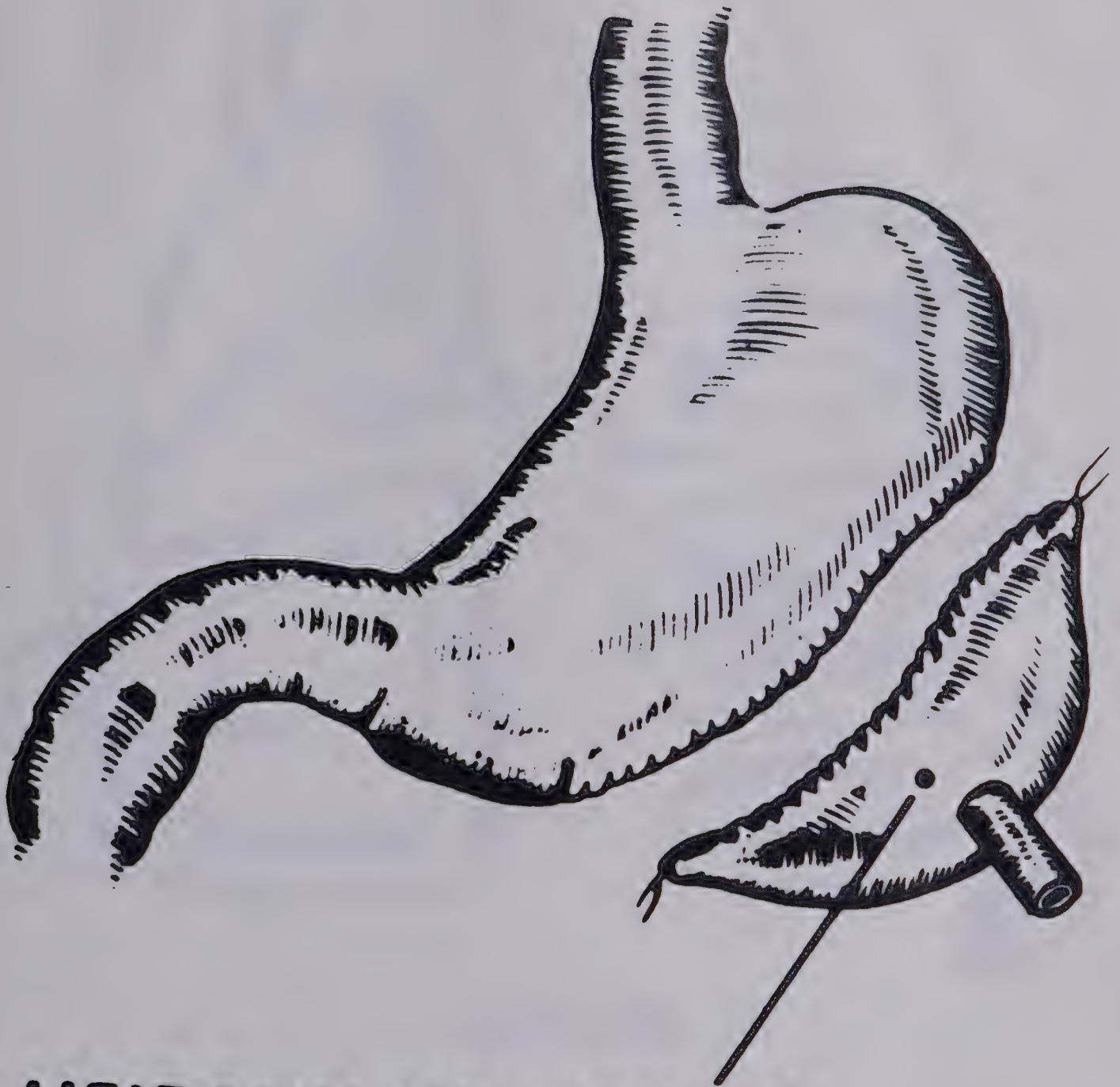
A search of the abdominal cavity was first made to exclude any unsuspected pathology. When none was found, the serosa of the stomach was exposed by gentle displacement of the omentum, and non-crushing clamps applied to contain a generous wedge from the fundic area of the greater curvature, the point of the wedge being equidistant from both curvatures. Defects were created in the omentum to enable the wedge to retain a blood supply when separated from the main stomach, and occasionally the ligation and division of a marginal artery was necessary to make these openings large enough.

The mucosa pouting through the teeth of the clamps on the main stomach was then sewn together with 3-0 catgut, the clamps removed, and the serosal edges co-apted with a running suture also of 3-0 chromic catgut to bury the mucosal suture line. A similar procedure was performed on the resected wedge, except that before the pouch was completely closed, a stainless steel cannula was placed inside it, and the end brought out through a separate incision. The cannulated pouch was then allowed to rest without tension against the internal abdominal wall, and the end of the cannula brought out through the abdominal wall in a suitable place to drain freely. Interrupted sutures were used to fix the pouch in this position, and after a final check for hemostasis, the abdomen was closed in layers.

## VI. Enterectomy (Figure 2)

The small intestine was delivered from the abdomen from the Ligament of Treitz to the junction with the cecum, and its length



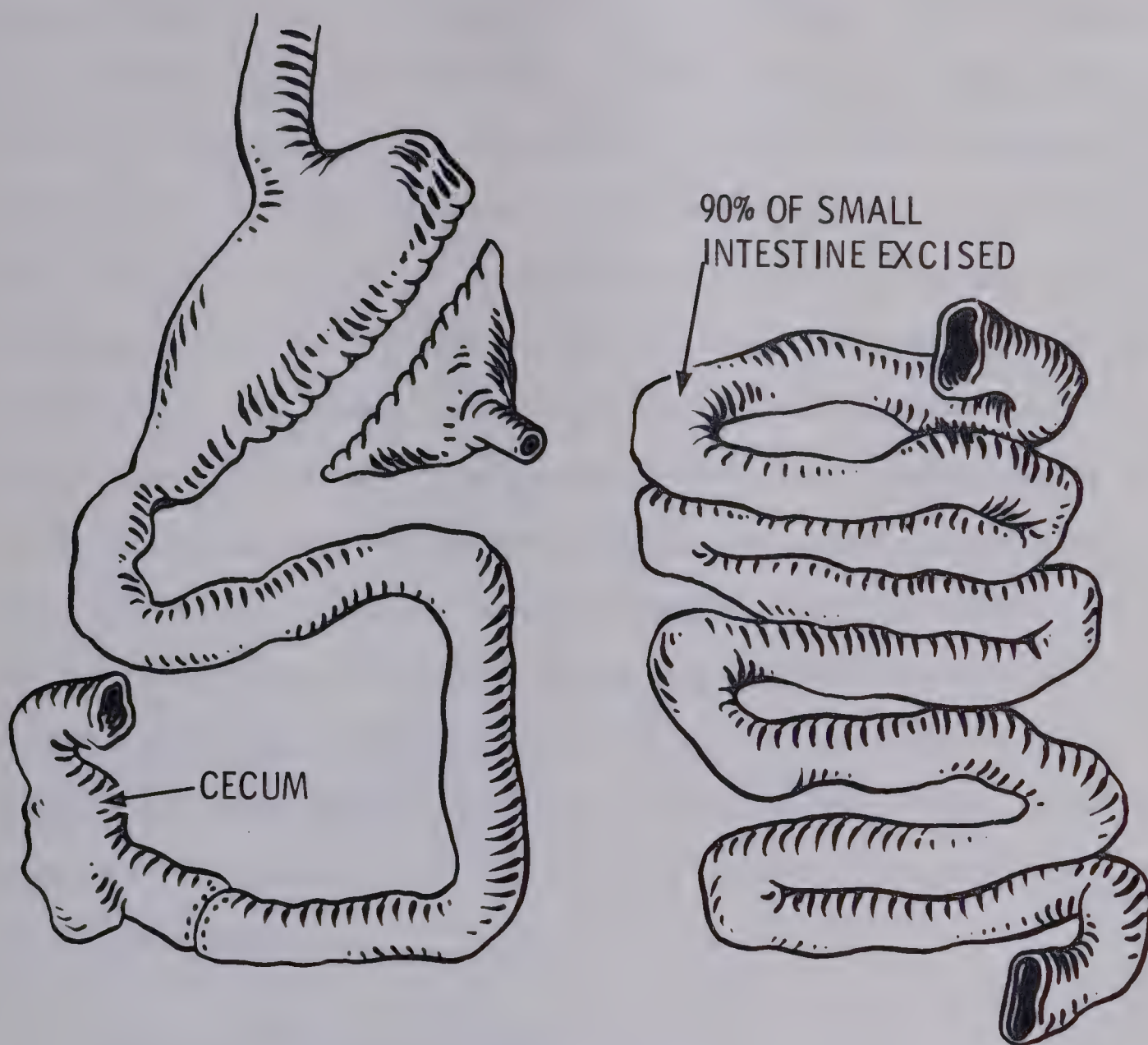


## HEIDENHAIN POUCH

Fig. 1.--Heidenhain Pouch







ENTERECTOMY

Fig. 2.--Massive Enterectomy





measured with a ruler. The average length was 300 cm. Five per cent of this length was measured distally from the Ligament of Treitz, and five per cent proximally from the ileocecal junction, and non-crushing clamps applied at these two places. The mesenteric vessels lying between these two points were ligated in continuity and divided, and the intestine between these two points resected, to include the wall that was held in the teeth of the clamps. A two layer end-to-end anastomosis was then performed, using 4-0 chromic catgut for the mucosa, and 3-0 silk for the serosal layer. The mesenteric defect was repaired with interrupted sutures of 3-0 chromic catgut to prevent possible herniation. The anastomotic lumen was checked for patency, and the anastomosed bowel for viability. Hemostasis was secured, and the abdomen closed in layers, using an absorbable subcuticular suture for the skin to obviate the need for subsequent suture removal with its disturbing effect on the experimental subject.

#### VII. Segmental Reversal (Figure 3)

The shortened small intestine was withdrawn from the abdominal cavity after freeing any adhesions tethering it. An eight centimeter length was selected immediately distal to the Ligament of Treitz, the vascular supply of which would lend itself to torsion without compromising it. On either side of these vessels, defects were created in the mesentery parallel with the vessels, and the integrity of the blood supply confirmed by prolonged inspection. Paired non-crushing clamps were then applied to the intestine immediately distal to these defects,



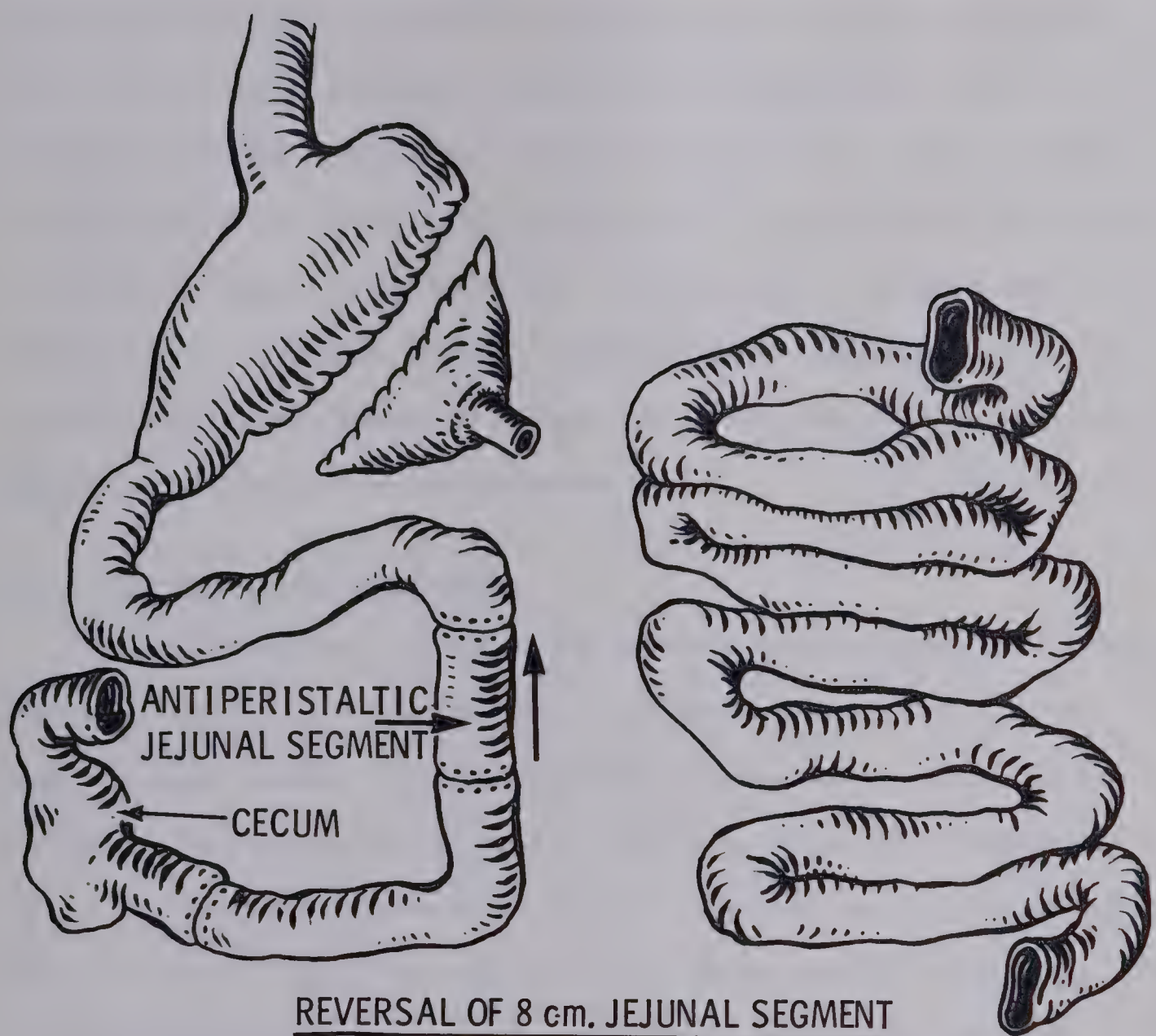


Fig. 3.--Insertion of an 8 cm. Antiperistaltic Segment



where the surface had been gently cleared of fat. The bowel was then cut across at these two places as a continuation of the two mesenteric rents, turned on its vascular pedicle through 180 degrees, and alimentary continuity restored by end-to-end anastomosis. Chromic catgut 4-0 was used to approximate the mucosa, and 3-0 silk for serosal layer, all these sutures being interrupted. The patency of the lumen was established by palpation, and the viability of the segment by inspection before the abdomen was closed in layers, using a subcuticular chromic catgut suture for skin closure.

#### VIII. Postoperative Management

Immediately at the conclusion of every surgical procedure, the dogs were covered with a spare drape, and the operating room lights used to supply warmth while they regained consciousness. This was instrumental in diminishing the violent shivering known to accompany recovery from Nembutal anaesthesia in dogs. When the orbital reflex had returned, and the level of anaesthesia had become sufficiently light for the swallowing reflex to be demonstrable, the dog was extubated. On recovery of consciousness, the animals were returned to their runs.

Fluids were given intravenously for the first three days after surgery, as 30 ml./kg. of 5% dextrose saline. During the third day, water was offered in a bowl, which the dogs invariably took well by mouth. Milk, pabulum, and Heinz clear consomme were given as tolerated, and the dogs had resumed normal feeding by the sixth postoperative day. One gram of calcium carbonate was included in the diet to lessen the inevitable diarrhea.





To minimize the distortion of results by infection, prophylactic antibiotics were used. Ten millograms per kilogram of "Fortimycin", a mixture of penicillin and streptomycin, were given before surgery, and daily thereafter for three days. Normal exercise was resumed at this time.

No testing was undertaken until three weeks after every surgical procedure, and the dog was carefully assessed during this recovery time. Pouch secretions were then collected when the dog had completely recovered from the insult.

Gastric emptying times were measured radiologically, during the control period, following enterectomy, and after insertion of the anti-peristaltic segment. Abdominal x-rays were taken immediately after the dog had eaten a meal consisting of 50 gm. of commercial dog meat mixed with 50 ml. of liquid barium. Hourly x-rays were taken thereafter, and the end point taken as the time when only traces of the mixture remained in the stomach.

#### IX. Collection of Samples

Bard rubber bladders were fitted with an attachment enabling them to be fixed to the metal cannula draining the secretions of the Heidenhain Pouch to the exterior. To obtain the twenty-four hour samples, the bladder was fitted to the cannula at 5:00 p.m. one evening, and removed at 5:00 p.m. the following evening. The bladders were protected by muzzling the dogs, which were only removed for feeding, while the animals were under observation. The twenty-four collections



took place under normal conditions of activity in the animal house. For the fed collections, the dogs were given eight ounces of Dr. Ballard's dog food twice during the day.

For the eight hour awake collections, the bags were fixed on at 9:00 a.m., emptied at hourly intervals until 5:00 p.m., and protected by muzzling the dogs.

For the eight hour anaesthetized collections, the dogs were given Nembutal intravenously, 30 mg./kg. and an endotracheal tube inserted. They were laid on their left side, with the cannula draining into the rubber bladder, and the contents emptied and measured hourly. Hydration was maintained by intravenous infusion of 5% dextrose saline at 5 ml./kg./hr. For the fed anaesthetized collections, a homogenate of 120 gm. of Dr. Ballard's dog food and 80 ml. distilled water was infused into the stomach via orogastric tube at the end of the second hour.

At every collection, the bladders were carefully inspected for leakage or damage, and that sample discarded if any were found.

#### X. Laboratory Procedures

Determination of gastric acidity.--- The volume of every sample was measured and recorded. The quantity of free and total acid in the secretions was determined by the following method: one milliliter of the sample was pipetted into a titration vessel in an autoburette, and the pH measured automatically by a pH meter.



The radiometer automatic titrator was then connected to the autoburette, and N/10 sodium hydroxide automatically added to the sample until a pH of 4.0 was reached, at which time the amount of free acid was indicated on a dial on the autoburette.

At this point, another circuit was set in operation, which continued the titration to pH 7.0, when the amount of total acid present in the sample appeared on the same scale on the autoburette.

No indicator was used, because the amount of N/10 sodium hydroxide added to bring the pH to 4.0 and 7.0 respectively was directly proportional to the amounts of free and total acid present in the sample.



## RESULTS

### I. Twenty-Four Hour Heidenhain Pouch Secretions

Control.-- The mean total twenty-four hour postprandial Heidenhain Pouch secretion of 74 ml. in this category is in keeping with the range found by other investigators. The mean free acid concentration was 6.5 m.Eq./vol. and the mean total acid concentration was 7.5 m.Eq./vol.

The mean twenty-four hour total fasting Heidenhain Pouch secretion of 65 ml. is within the expected range, and is predictably less than the postprandial mean volume. There was a corresponding decrease in the mean free acid concentration, which was 6.1 m.Eq./vol. and the mean total acid concentration, which was 6.5 m.Eq./vol.

After massive enterectomy.-- The mean total twenty-four hour total postprandial Heidenhain Pouch secretion rose to 162 ml., the mean free acid concentration to 21 m.Eq./vol. and the mean total acid concentration to 24 m.Eq./vol. (Figure 4). All three increments were statistically significant ( $p = 0.01$ ) (Table 1, 1<sup>S</sup>)\*

The mean total twenty-four hour fasting Heidenhain Pouch secretion rose to 90 ml. the mean free acid concentration to 9.5 m.Eq./vol. and the mean total acid concentration to 10.4 m.Eq./vol. (Figure 4). None of these increments was statistically significant (Table 2, 2<sup>S</sup>)\*

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\* Statistical analysis (Tables 1<sup>S</sup>-6<sup>S</sup>) appears at the end of this section.







### 24 HR. HEIDENHAIN POUCH SECRETION IN 6 DOGS

Fig. 4.--Effect of enterectomy and subsequent insertion of an antiperistaltic segment, on mean total twenty-four hour postprandial and fasting secretion. Both enterectomy and reversal significantly increased Heidenhain Pouch secretion in postprandial dogs ( $p = 0.01$ ) as compared to the controls. There was no significant increase in Heidenhain Pouch secretion after enterectomy in fasting dogs, but reversal resulted in a significant increase ( $p = 0.05$ ).



TABLE 1.--Mean Total Twenty-Four Hour Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). Statistically Significant Increases ( $p = 0.01$ ) were Noted in Heidenhain Pouch Secretory Volume, Free and Total Acid Concentrations, After Both Operative Procedures

	Control	Group A	P value <sup>‡</sup>	Group B	P value <sup>‡</sup>
Volume <sup>*</sup>	74.5	162.2	0.01	283.2	0.01
Free Acid <sup>†</sup>	6.48	20.64	0.01	39.37	0.01
Total Acid <sup>†</sup>	7.54	23.77	0.01	40.98	0.01

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of the change as compared with control figures.



TABLE 2.--Mean Total Twenty-Four Hour Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment, No Statistically Significant Change Following Enterectomy, but After Insertion of the Reversed Segment, Significant Changes were Noted in Heidenhain Pouch Secretory Volume, Free and Total Acid Concentrations (p=0.05)

	Control	Group A	P value <sup>†</sup>	Group B	P value <sup>‡</sup>
Volume <sup>*</sup>	64.7	90.5	N.S.	203.2	0.05
Free Acid <sup>†</sup>	6.10	9.50	N.S.	23.72	0.05
Total Acid <sup>†</sup>	6.50	10.37	N.S.	27.36	0.05

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of the change as compared with control figures.





After segmental reversal.-- The mean total twenty-four hour postprandial Heidenhain Pouch secretion underwent a further rise, to 283 ml. The mean free acid concentration rose to 39 m.Eq./vol. and the mean total acid concentration rose to 41 m.Eq./vol. (Figure 4). All three increments were statistically significant as compared with the control secretions ( $p = 0.01$ ) (Table 1). Compared with the post-enterectomy secretions, the increases in the volume and free acid secretions were significant ( $p = 0.05$ ), but the increase in total acid concentration was not significant. (Table 1<sup>s</sup>)

The mean total twenty-four hour fasting Heidenhain Pouch secretions rose further to 203 ml. following insertion of an anti-peristaltic segment. The mean free acid concentration rose to 24 m.Eq./vol. and the mean total acid concentration rose to 27.4 m.Eq./vol. (Figure 4). Compared with the control figures, all three increments were statistically significant ( $p = 0.05$ ) (Table 2). Compared with the postenterectomy figures, only the rise in mean total acid concentration was statistically significant ( $p = 0.05$ ) (Table 2<sup>s</sup>).

## II. Eight Hour Awake Heidenhain Pouch Secretions

Control.-- The mean total eight hourly postprandial Heidenhain Pouch secretion was 36.4 ml. The mean free acid concentration was 4.2 m.Eq./vol. and the mean total acid concentration was 4.5 m.Eq./vol.

The mean total eight hour fasting Heidenhain Pouch secretion was 9.5 ml. The mean free acid concentration was 0.27 m.Eq./vol. and the mean total acid concentration was 0.29 m.Eq./vol.



After massive enterectomy.-- The mean eight hour total post-prandial Heidenhain Pouch secretion decreased slightly to 35.8 ml. The mean free acid concentration however rose to 4.7 m.Eq./vol. and the mean total acid concentration rose to 4.9 m.Eq./vol. (Figure 5). None of these changes was statistically significant (Table 3, 3<sup>S</sup>).

The mean eight hour total fasting Heidenhain Pouch secretion also decreased to 8.6 ml. Despite this fall in secretory volume, the mean free acid concentration, however, rose to 0.44 m.Eq./vol. and the mean total acid concentration rose to 0.51 m.Eq./vol. (Figure 5). None of these changes was statistically significant. (Table 4, 4<sup>S</sup>).

After segmental reversal.-- The mean total eight hour post-prandial Heidenhain Pouch secretion underwent another small decrease after insertion of an antiperistaltic segment of small intestine, falling to 34.34 ml. The mean free acid concentration now fell to below the control level, reaching 3.96 m.Eq./vol. while the mean total acid concentration fell to 4.21 m.Eq./vol.--also less than the control figure (Figure 5). None of these changes was statistically significant (Tables 3, 3<sup>S</sup>).

The mean total eight hour fasting Heidenhain Pouch secretion remained unchanged at 8.65 ml. after segmental reversal (Figure 5). The mean free and total acid concentrations were also unaffected by this procedure, remaining at 0.44 m.Eq./vol. and 0.51 m.Eq./vol. (Table 4, 4<sup>S</sup>).



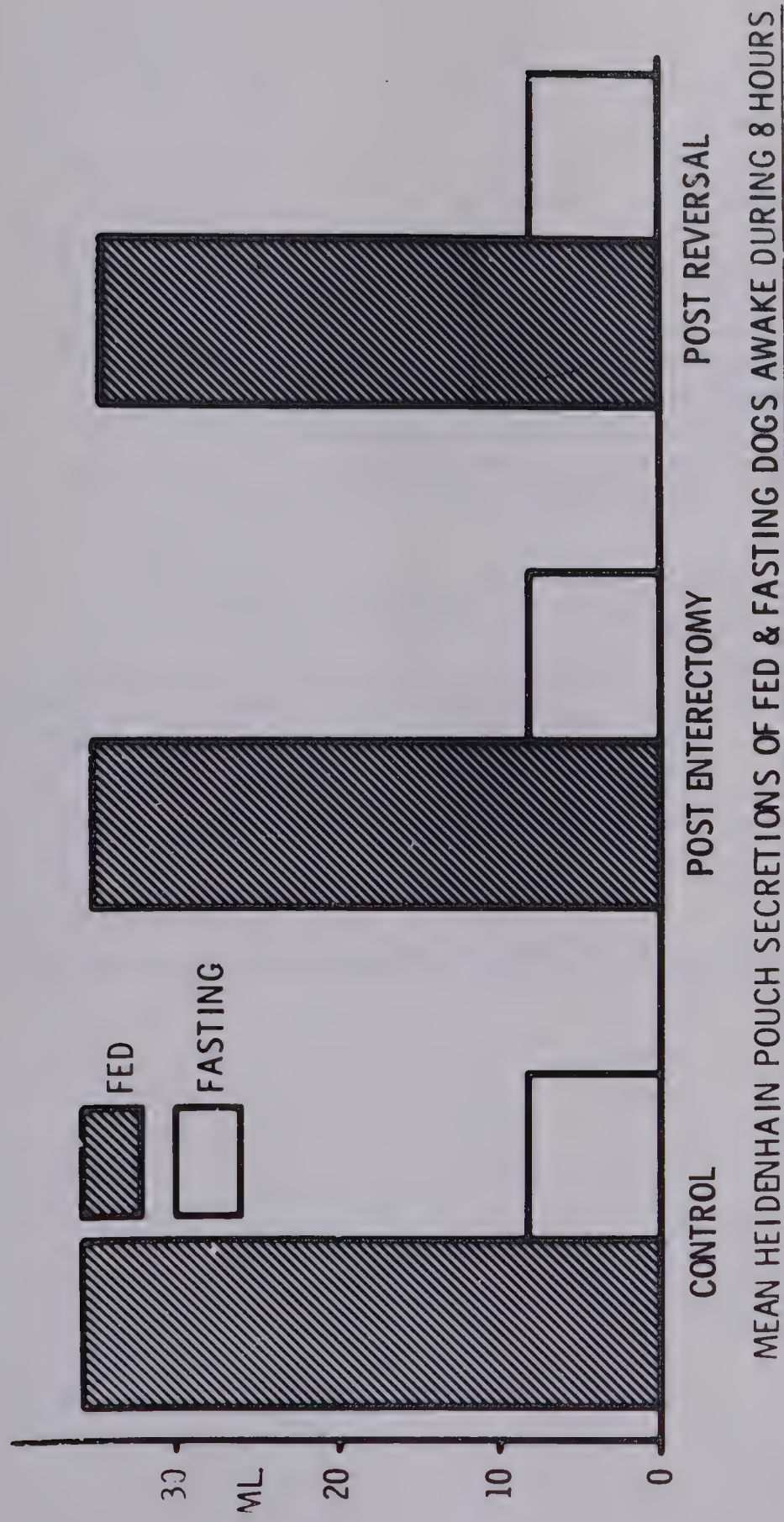


Fig. 5.--Effect of enterectomy and subsequent insertion of an antiperistaltic segment on mean total eight hour Heidenhain Pouch secretory volumes in awake dogs. No significant changes were observed after either procedure as compared to the controls.





TABLE 3.--Mean Total Eight Hour Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A) and Dogs with an Antiperistaltic Jejunal Segment (Group B). None of the Heidenhain Pouch Secretory Changes Following Either Procedure was Statistically Significant

	Control	Group A	P value <sup>†</sup>	Group B	P value <sup>†</sup>
Volume <sup>*</sup>	36.4	35.8	N.S.	34.3	N.S.
Free Acid <sup>†</sup>	4.24	4.69	N.S.	3.96	N.S.
Total Acid <sup>†</sup>	4.45	4.88	N.S.	4.21	N.S.

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of the change as compared with control figures.





TABLE 4.--Mean Total Eight Hour Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). No Statistically Significant Secretory Change was Observed After Either Procedure

	Control	Group A	P value <sup>†</sup>	Group B	P value <sup>‡</sup>
Volume <sup>*</sup>	9.5	8.7	N.S.	8.7	N.S.
Free Acid <sup>†</sup>	0.27	0.43	N.S.	0.44	N.S.
Total Acid <sup>†</sup>	0.29	0.50	N.S.	0.51	N.S.

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of the change as compared with control figures.



### III. Eight Hour Anaesthetized Heidenhain Pouch Secretions

Control.-- The mean total eight hour postprandial Heidenhain Pouch secretion was 34.1 ml. The mean free acid concentration was 3.94 m.Eq./vol., and the mean total acid concentration was 4.13 m.Eq./vol.

The mean total eight hour fasting Heidenhain Pouch secretion was 16.7 ml. The mean free acid concentration was 0.67 m.Eq./vol. and the mean total acid concentration 0.80 m.Eq./vol.

After massive enterectomy.-- After enterectomy, the mean total eight hour postprandial Heidenhain Pouch secretion rose to 52.6 ml. The mean free acid concentration rose to 6.70 m.Eq./vol. and the mean total acid concentration to 6.96 m.Eq./vol. (Figure 6). None of these changes was statistically significant (Tables 5, 5<sup>S</sup>).

The mean total eight hour fasting Heidenhain Pouch secretion rose to 28.5 ml. after enterectomy. The mean free acid concentration rose markedly to 2.73 m.Eq./vol. and so did the mean total acid concentration, to 2.88 m.Eq./vol. (Figure 6). None of these changes was statistically significant (Tables 6, 6<sup>S</sup>).

After segmental reversal.-- Following insertion of the antiperistaltic segment, the mean total eight hour postprandial Heidenhain Pouch secretion rose to 73.9 ml. The mean free acid concentration rose to 9.94 m.Eq./vol., and the mean total acid concentration rose to 10.02 m.Eq./vol. (Figure 6).

The mean total eight hour fasting Heidenhain Pouch secretion after insertion of an antiperistaltic segment remained unchanged at 28.55 ml. Similarly, the free and total acid concentrations were unaffected by the procedure. (Tables 6, 6<sup>S</sup>).



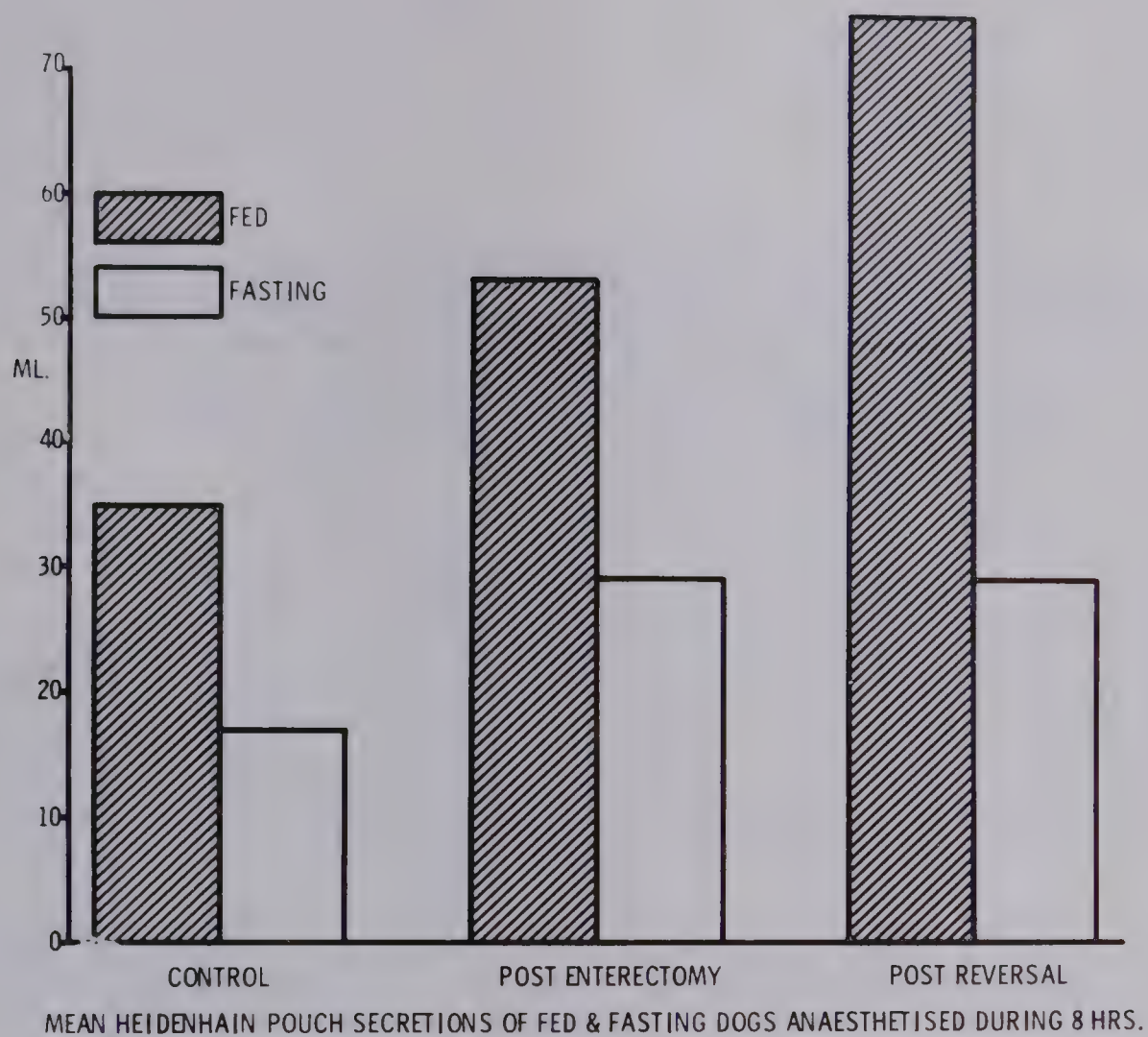


Fig. 6.--Effect of enterectomy and subsequent insertion of an antiperistaltic segment on mean total eight hour Heidenhain Pouch secretory volumes in anaesthetized dogs. No statistically significant changes were observed after either procedure.





TABLE 5.--Mean Total Eight Hour Anaesthetized Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B).  
None of the Secretory Changes Following Either Procedure was Statistically Significant

	Control	Group A	P value <sup>‡</sup>	Group B	P value <sup>‡</sup>
Volume <sup>*</sup>	34.1	52.6	N.S.	74.0	N.S.
Free Acid <sup>†</sup>	3.94	6.70	N.S.	9.94	N.S.
Total Acid <sup>†</sup>	4.13	7.00	N.S.	10.03	N.S.

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of the change as compared with control figures.



TABLE 6.--Mean Total Eight Hour Anaesthetized Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs, Enterectomized Dogs (Group A), and Dogs with an Antiperistaltic Jejunal Segment (Group B). None of the Secretory Changes Following Either Procedure was Found To Be Statistically Significant

	Control	Group A	P value <sup>‡</sup>	Group B	P value <sup>‡</sup>
Volume <sup>*</sup>	16.7	28.5	N.S.	28.5	N.S.
Free Acid <sup>†</sup>	0.67	2.72	N.S.	2.72	N.S.
Total Acid <sup>†</sup>	0.80	2.88	N.S.	2.88	N.S.

\* Volume in ml.

† Acid in m.Eq./vol.

‡ Statistical significance of the change as compared with control figures.



#### IV. Body Weights

At the beginning of the experiment, in January, 1969, the mean body weight of the dogs equipped with their Heidenhain Pouch, was 19.2 kilos. Immediately after massive enterectomy, the body weights of the dogs began to decline steadily, in the way described by previous investigators. (1) By the 49th postenterectomy day, in March 1969, the mean weight had fallen to 15.8 kilos (82% of the original figure), and was continuing to fall.

It was at this stage that the antiperistaltic segment was inserted, with the downward trend well established, but while the dogs were still able to withstand surgery. The weight loss continued, but at a reduced rate. By the 49th postreversal day, in May, 1969, the mean weight of the dogs had levelled off at 14.4 kilos (75% of the original figure). Two weeks later, at the conclusion of the experiment, this mean weight had not changed. (Figure 7).

#### V. Gastric Emptying Times

Controls.-- The mean transit time for a mixture of 50 gm. meat and 50 ml. of barium to empty from the stomach in the control group of dogs was three hours. The stomach was considered empty when only traces of the meal remained visible in the lumen. Figure 8 shows the plate taken shortly after dog 1359 had swallowed the mixture, on the left; and on the right, the three hour plate, when the emptying process is complete.



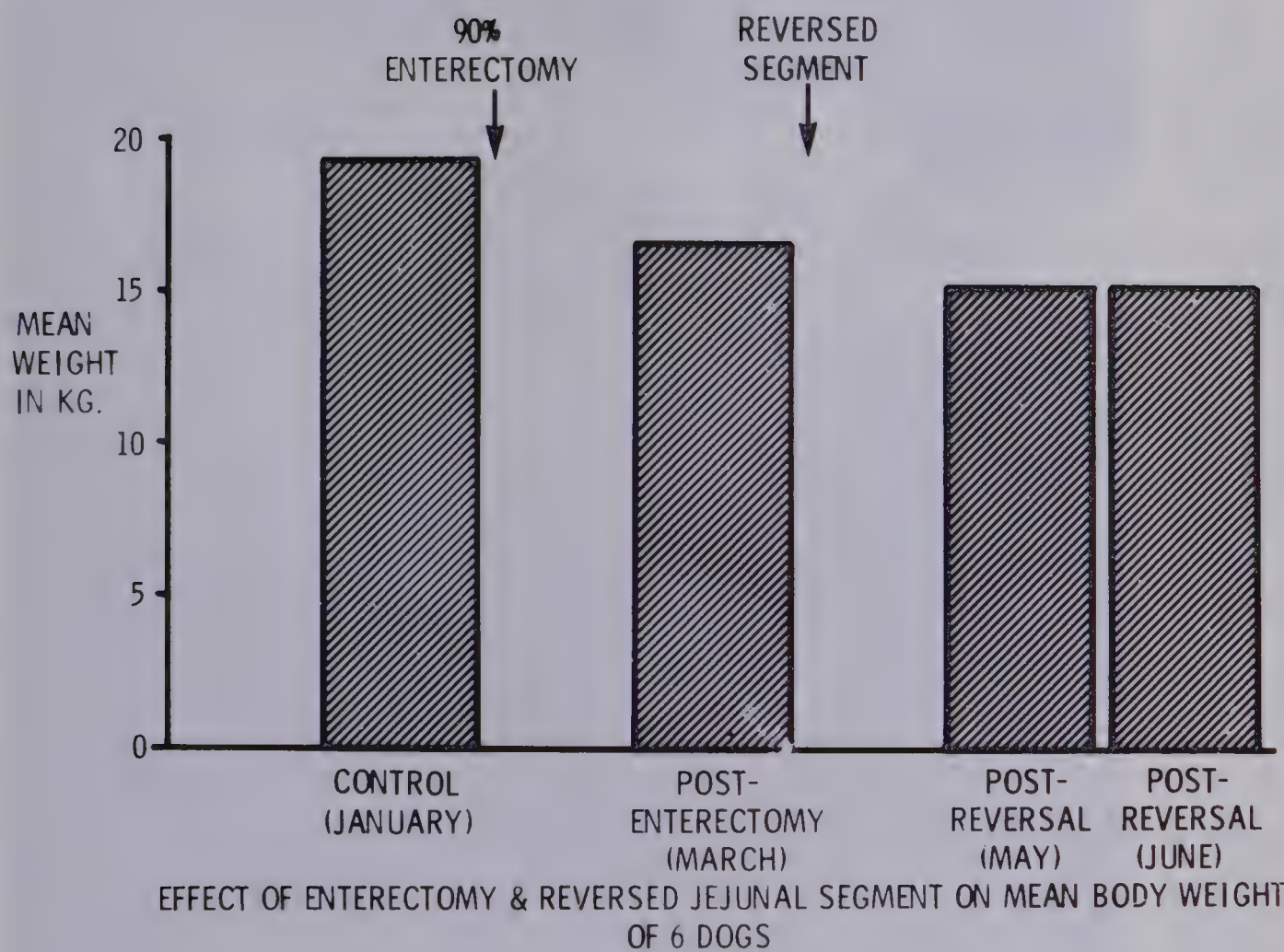


Fig. 7.--Comparison of the mean body weights of dogs before enterectomy, two months after massive enterectomy, and two and three months after reversal of a jejunal segment.





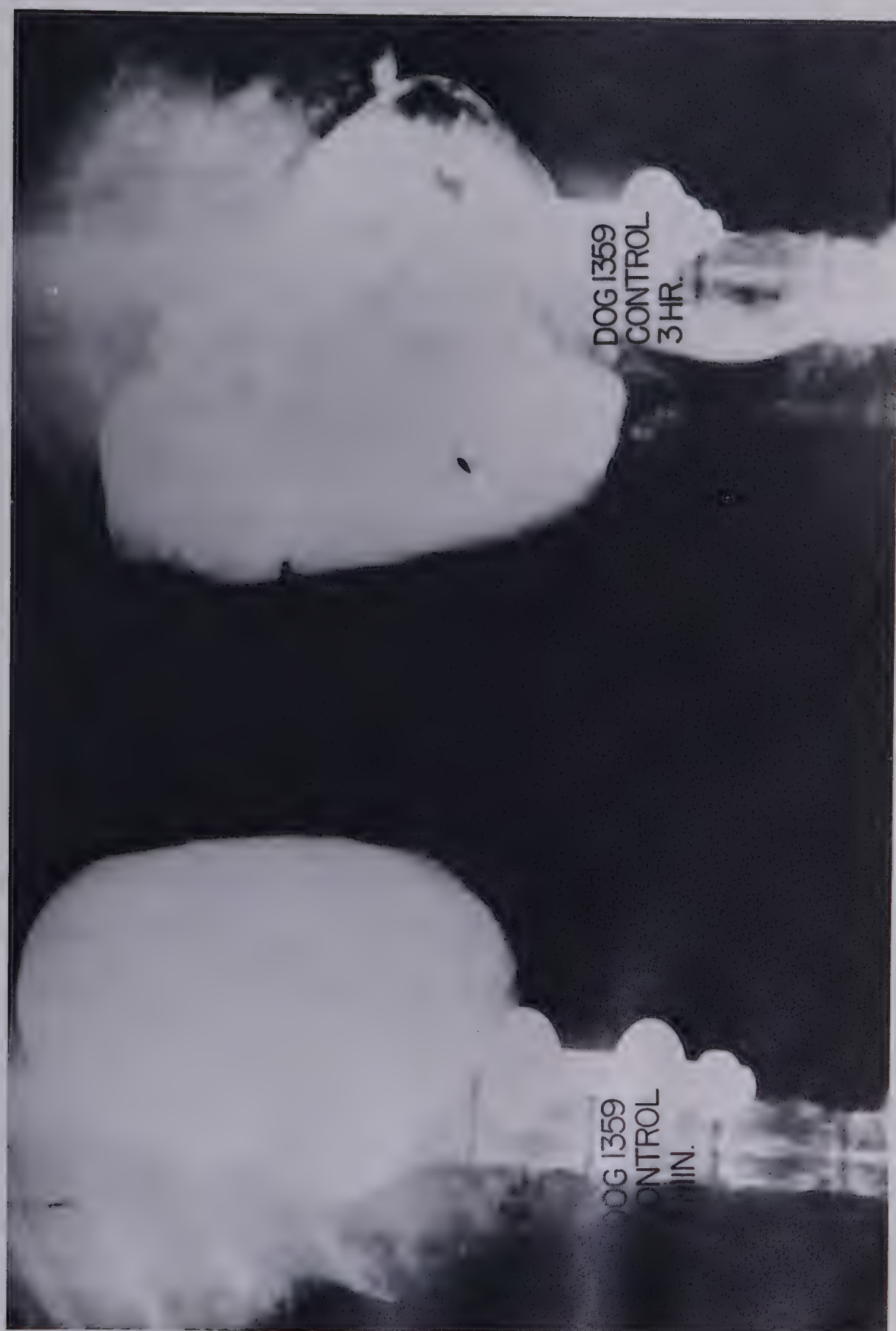


Fig. 8.--Barium x-rays of control dog's (1359) gastric emptying time. The plate on the left shows the stomach a few minutes after the dog had swallowed the barium mixture. The plate on the right shows the same stomach empty three hours later.



After massive enterectomy.--- Following enterectomy, the mean gastric emptying time was unchanged from the control figure of three hours. On the left, Figure 9 again shows the stomach of the enterectomized dog 1359 a few minutes after swallowing the same quantity of the barium mixture; and the same stomach three hours later, on the right, when only traces of the meal are visible within the stomach.

After segmental reversal.--- Following insertion of an anti-peristaltic jejunal segment, transit time was delayed. Figure 10 shows on the left, the stomach of dog 1359 soon after swallowing the same amount of the barium mixture. The x-ray on the right, taken three hours later, shows a large proportion of the meal remaining in the stomach. Serial x-rays were taken hourly, and it was not until the six hour plate that the emptying of the stomach was seen to be near completion (Figure 11). The postreversal emptying times were spread over five to seven hours, six being the mean. Dog 1359 was typical.

The profuse diarrhea that followed massive enterectomy, and persisted in spite of oral calcium carbonate therapy (1 gm. daily in the food), was markedly reduced following the insertion of an anti-peristaltic segment, and in some cases, the dogs produced semi-formed stools.



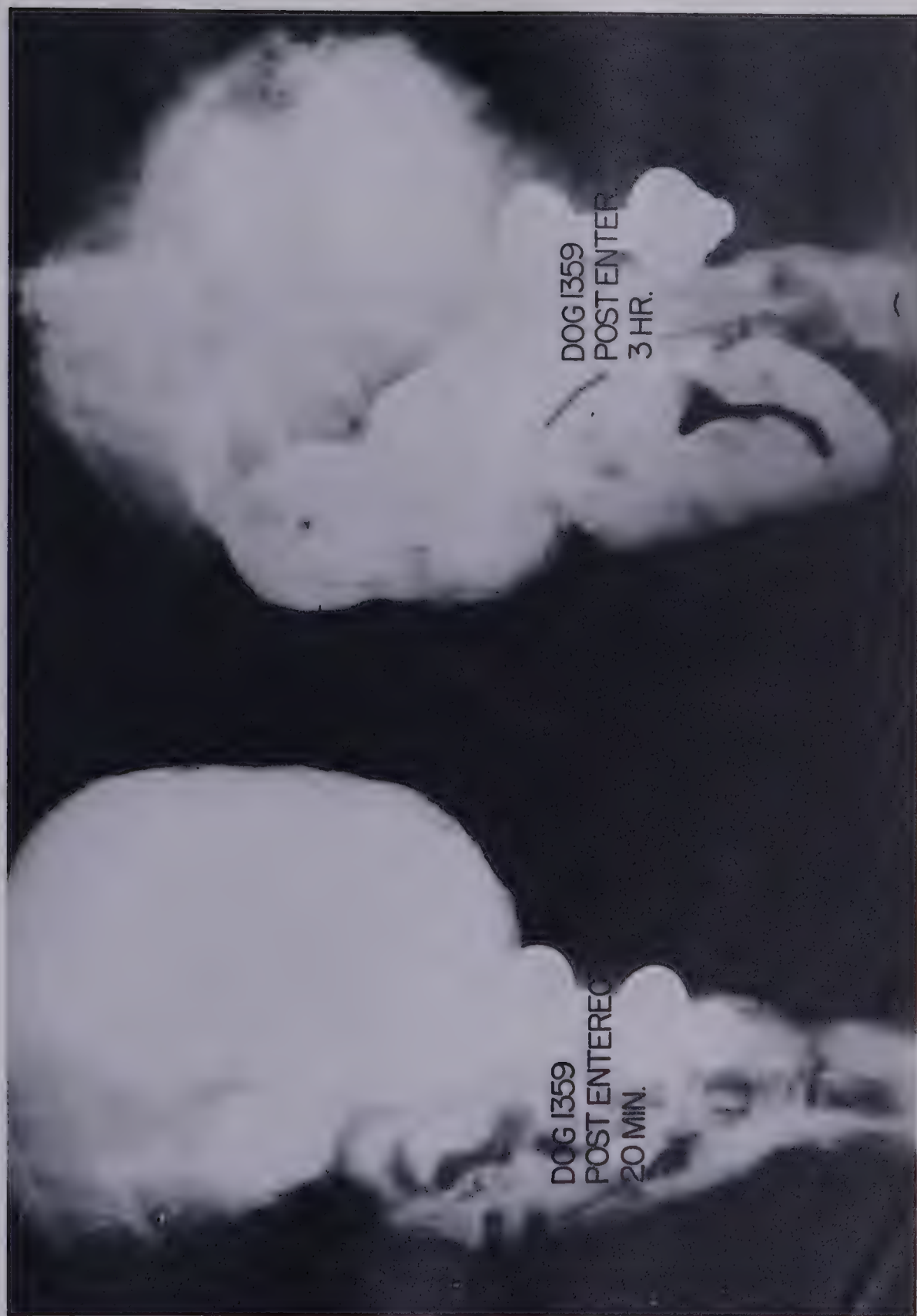


Fig. 9.--Barium x-rays of dog 1359 after enterectomy. The plate on the left shows the stomach a few minutes after the dog had swallowed the barium mixture. The plate on the right shows the same stomach empty three hours later.





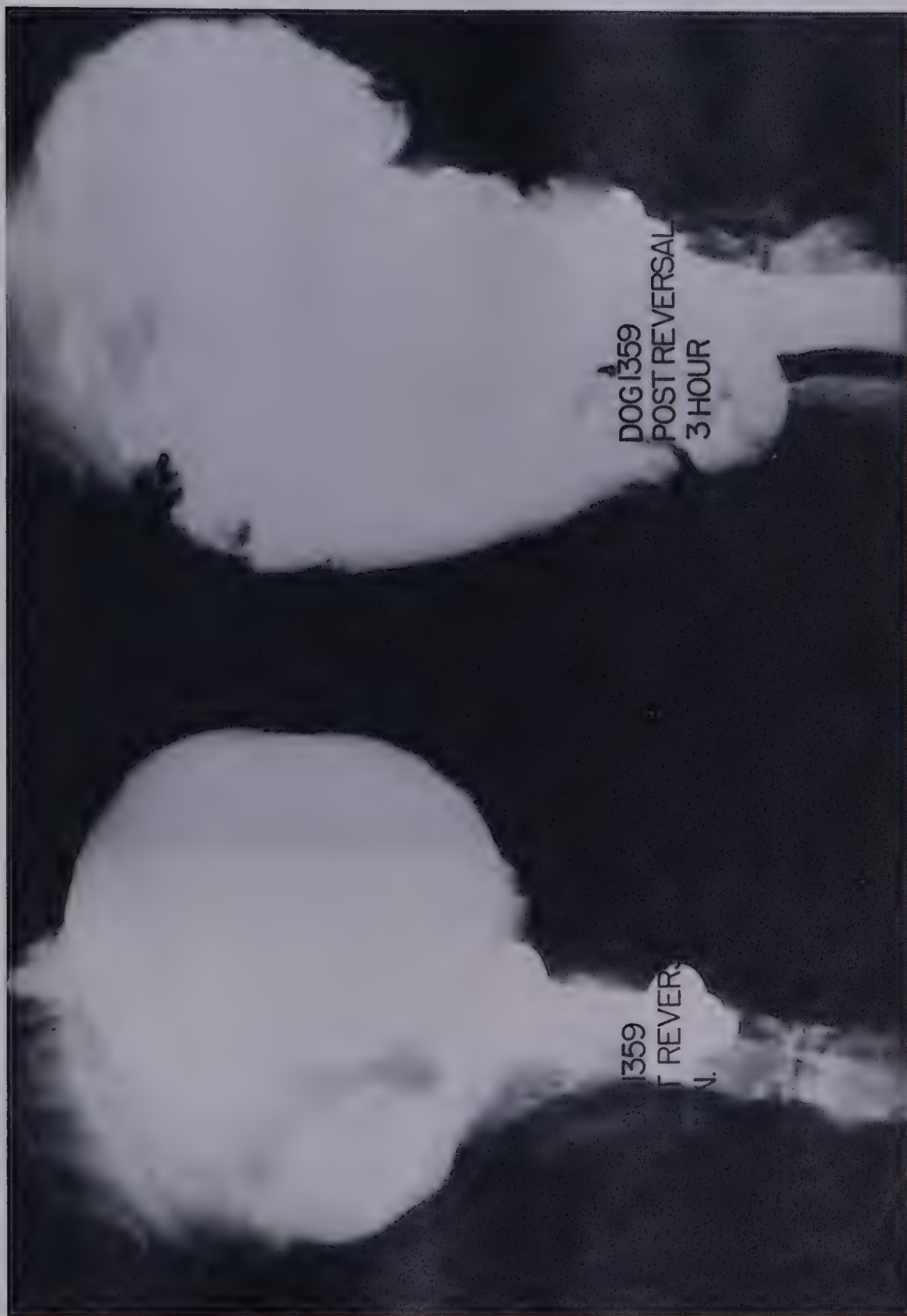


Fig. 10.--Barium x-rays of dog 1359 after insertion of an anti-peristaltic segment. The plate on the left shows the stomach a few minutes after the dog had swallowed the barium mixture. The plate on the right shows the same stomach remaining partially full three hours later.





Fig. 11.--Barium x-ray of dog 1359 after insertion of an anti-peristaltic segment. The stomach is almost empty of the barium mixture at six hours after its ingestion, demonstrating a long delay in gastric emptying after segmental reversal. Also see Figure 10.



## FOOTNOTES

<sup>1</sup>REUL, G.J., and ELLISON, E.H. Effect of 75% distal small bowel resection on gastric secretion. Am. J. Surg., 111:772, 1966.



TABLE 1<sup>s</sup>.--Statistical Analysis of the Changes in Twenty-four Hour Total Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3)

	Means			E1:E2				E1:E3				E2:E3			
	E1 <sup>*</sup>	E2 <sup>†</sup>	E3 <sup>‡</sup>	Confidence interval	T-value	Signi- fiance	Confidence interval	T-value	Signi- fiance	Confidence interval	T-value	Signi- fiance			
Volume	74.500	162.167	283.167	174.625	-0.708	1 %	363.952	-53.381	4.105	1 %	228.052	-13.948	2.396	5 %	
Free Acid	6.479	20.640	39.367	-27.032	-1.290	1 %	-57.387	- 8.389	4.100	1 %	-35.916	- 1.537	2.309	5 %	
Total Acid	7.542	23.767	40.983	-29.383	-3.067	1 %	-57.765	- 9.117	4.199	1 %	-34.456	0.024	2.117	N.S.	

\* Control.

† Postenterectomy.

‡ Post reversal.





TABLE 2<sup>s</sup> .--Statistical Analysis of the Changes in Twenty-four Hour Total Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations in Control Dogs (E1), Enterectomized Dogs (E2), and Dogs with an Antiperistaltic Jejunal Segment (E3)

	Means			E1:E2			E1:E3			E2:E3		
	E1 <sup>*</sup>	E2 <sup>†</sup>	E3 <sup>‡</sup>	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance
Volume	64.667	90.500	203.200	-78.492 26.825	1.093	N.S.	251.935 -25.132	2.764	5 %	231.280 5.880	2.150	N.S.
Free Acid	6.100	9.502	23.720	-9.895 3.092	1.167	N.S.	-33.712 -1.528	2.477	5 %	-30.521 2.085	1.973	N.S.
Total Acid	6.500	10.375	27.360	-10.618 2.868	1.280	N.S.	-37.149 - 4.571	2.897	5 %	-33.520 0.450	2.324	5 %

\* Control.

† Postenterectomy.

‡ Post reversal.



TABLE 3<sup>5</sup>.--Statistical Analysis of the Changes in Eight Hour, Hourly Awake Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3)

	Means			E1:E2				E1:E3				E2:E3				
	E1 <sup>‡</sup>	E2 <sup>†</sup>	E3 <sup>‡</sup>	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance	
Volume	0.043	2.240	3.050	-4.395	0.000	2.131	N.S.	-5.243	-0.771	2.960	2.960	5 %	-3.803	2.183	0.580	N.S.
	0.099	4.570	4.017	-9.319	0.377	1.966	N.S.	-7.376	-0.460	3.519	3.519	1 %	-5.088	6.194	0.210	N.S.
	3.400	7.080	6.300	-8.695	1.335	1.564	N.S.	-9.207	3.407	1.012	1.012	N.S.	-5.657	7.217	0.260	N.S.
	5.514	6.400	6.350	-7.507	5.735	0.285	N.S.	-8.679	7.008	0.235	0.235	N.S.	-5.255	5.355	0.020	N.S.
	6.700	5.100	8.167	-4.782	7.982	0.534	N.S.	-10.040	7.106	0.377	0.377	N.S.	-7.327	1.194	1.544	N.S.
	6.671	4.790	2.505	-6.031	9.794	0.507	N.S.	-5.818	14.151	0.918	0.918	N.S.	-1.320	5.890	1.360	N.S.
	6.657	3.810	1.583	-5.443	11.138	0.732	N.S.	-5.945	16.093	1.013	1.013	N.S.	0.092	4.362	2.237	5 %
	7.357	1.840	2.367	-3.251	14.285	1.341	N.S.	-6.960	16.941	0.919	0.919	N.S.	-1.466	0.413	1.202	N.S.
	36.441	35.830	34.339													
Free Acid	0.000	0.265	0.293	-0.542	0.012	2.036	N.S.	-0.545	-0.042	2.567	2.567	5 %	-0.392	0.335	0.167	N.S.
	0.000	0.586	0.440	-1.294	0.122	1.764	N.S.	-0.811	-0.069	2.609	2.609	5 %	-0.682	0.974	0.378	N.S.
	0.186	0.918	0.728	-1.517	0.052	1.991	N.S.	-1.484	0.398	1.269	1.269	N.S.	-0.881	1.262	0.381	N.S.
	0.560	0.818	0.810	-1.253	0.738	0.551	N.S.	-1.449	0.949	0.459	0.459	N.S.	-0.829	0.844	0.019	N.S.
	0.806	0.685	1.013	-0.892	1.123	0.256	N.S.	-1.528	1.113	0.346	0.346	N.S.	-1.004	0.348	1.042	N.S.
	0.894	0.629	0.330	-0.987	1.517	0.452	N.S.	-1.014	2.143	0.787	0.787	N.S.	-0.251	0.849	1.165	N.S.
	0.849	0.477	0.165	-0.920	1.662	0.613	N.S.	-1.038	2.406	0.874	0.874	N.S.	0.010	0.615	2.215	5 %
	0.949	9.317	0.148	-0.801	2.064	0.939	N.S.	-1.112	2.712	0.921	0.921	N.S.	-0.154	0.491	1.123	N.S.
	4.244	4.695	3.960													
Total	0.000	0.274	0.312	-0.561	0.013	2.033	N.S.	-0.575	-0.049	2.608	2.608	5 %	-0.416	0.340	0.215	N.S.
	0.000	0.579	0.517	-1.247	0.090	1.844	N.S.	-0.899	-0.134	2.971	2.971	5 %	-0.730	0.854	0.168	N.S.
	0.216	0.964	0.763	-1.551	0.055	1.985	N.S.	-1.521	0.427	1.237	1.237	N.S.	-0.883	1.284	0.397	N.S.
	0.607	0.848	0.845	-1.279	0.796	0.496	N.S.	-1.483	1.007	0.421	0.421	N.S.	-0.842	0.849	0.009	N.S.
	0.849	0.722	1.063	-0.891	1.144	0.265	N.S.	-1.552	1.122	0.354	0.354	N.S.	-1.029	0.346	1.065	N.S.
	0.917	0.657	0.347	-1.010	1.530	0.436	N.S.	-1.027	2.168	0.786	0.786	N.S.	-0.253	0.874	1.182	N.S.
	0.883	0.499	0.177	-0.931	1.698	0.622	N.S.	-1.046	2.458	0.887	0.887	N.S.	0.013	0.632	2.236	5 %
	0.979	0.338	0.185	0.805	2.087	0.945	N.S.	-1.134	2.721	0.906	0.906	N.S.	-0.181	0.486	0.983	N.S.
	4.451	4.881	4.209													

\* Control.

† Postenterectomy.

‡ Post reversal



TABLE 4<sup>S</sup>.--Statistical Analysis of the Changes in Eight Hour, Hourly Awake Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3)

	Means			E1:E2				E1:E3				E2:E3			
	E1 <sup>*</sup>	E2 <sup>†</sup>	E3 <sup>‡</sup>	Confidence interval	T-value	Significance		Confidence interval	T-value	Significance		Confidence interval	T-value	Significance	
Volume	1.575	0.736	0.736	-1.640	3.317	0.714	N.S.	-1.640	3.317	0.714	N.S.	-1.264	1.704	0.316	N.S.
	1.212	1.573	1.573	-2.930	2.210	0.296	N.S.	-2.930	2.210	0.296	N.S.	-2.461	3.539	0.383	N.S.
	0.925	1.073	1.073	-2.026	1.731	0.166	N.S.	-2.026	1.731	0.166	N.S.	-3.729	1.275	1.046	N.S.
	1.325	0.945	0.945	-0.644	1.403	0.782	N.S.	-0.644	1.403	0.782	N.S.	-2.217	0.341	1.563	N.S.
	0.762	1.209	1.209	-1.848	0.955	0.672	N.S.	-1.848	0.955	0.672	N.S.	-5.126	1.377	1.229	N.S.
	0.987	0.882	0.882	-0.939	1.150	0.213	N.S.	-0.939	1.150	0.213	N.S.	-1.710	1.207	0.368	N.S.
	1.212	1.036	1.036	-0.931	1.283	0.336	N.S.	-0.931	1.283	0.336	N.S.	-2.286	0.425	1.463	N.S.
	1.462	1.200	1.200	-0.644	1.169	0.611	N.S.	-0.644	1.169	0.611	N.S.	-1.845	0.711	0.945	N.S.
Total	9.460	8.654	8.654												
Free Acid	0.149	0.064	0.064	-0.217	0.386	0.593	N.S.	-0.217	0.386	0.593	N.S.	-0.126	0.217	0.568	N.S.
	0.063	0.168	0.168	-0.448	0.237	0.649	N.S.	-0.448	0.237	0.649	N.S.	-0.301	0.490	0.510	N.S.
	0.047	0.100	0.100	-0.287	0.183	0.470	N.S.	-0.287	0.183	0.470	N.S.	-0.383	0.290	0.296	N.S.
	0.000	0.043	0.043	-0.102	0.016	1.542	N.S.	-0.102	0.016	1.542	N.S.	-0.171	0.094	0.617	N.S.
	0.000	0.026	0.026	-0.073	0.022	1.152	N.S.	-0.073	0.022	1.152	N.S.	-0.582	0.154	1.239	N.S.
	0.000	0.007	0.007	-0.023	0.009	0.947	N.S.	-0.023	0.009	0.947	N.S.	-0.222	0.056	1.272	N.S.
	0.010	0.016	0.016	-0.044	0.033	0.316	N.S.	-0.044	0.033	0.316	N.S.	-0.269	0.067	1.280	N.S.
	0.000	0.015	0.015	-0.044	0.014	1.085	N.S.	-0.044	0.014	1.085	N.S.	-0.215	0.055	1.267	N.S.
Total	0.269	0.439	0.439												
Total Acid	0.153	0.068	0.068	-0.226	0.395	0.573	N.S.	-0.226	0.395	0.573	N.S.	-0.135	0.225	0.533	N.S.
	0.064	0.182	0.182	-0.478	0.241	0.695	N.S.	-0.478	0.241	0.695	N.S.	-0.321	0.512	0.489	N.S.
	0.050	0.110	0.110	-0.310	0.190	0.502	N.S.	-0.310	0.190	0.502	N.S.	-0.407	0.300	0.324	N.S.
	0.003	0.051	0.051	-0.115	0.018	1.549	N.S.	-0.115	0.018	1.549	N.S.	-0.180	0.096	0.653	N.S.
	0.001	0.036	0.036	-0.093	0.023	1.278	N.S.	-0.093	0.023	1.278	N.S.	-0.596	0.170	1.185	N.S.
	0.001	0.014	0.014	-0.036	0.011	1.100	N.S.	-0.036	0.011	1.100	N.S.	-0.232	0.062	1.226	N.S.
	0.012	0.025	0.025	-0.067	0.039	0.545	N.S.	-0.067	0.039	0.545	N.S.	-0.282	0.076	1.227	N.S.
	0.004	0.023	0.023	-0.053	0.017	1.090	N.S.	-0.053	0.017	1.090	N.S.	-0.232	0.057	1.288	N.S.
Total	0.288	0.509	0.509												

\* Control.

† Postenterectomy.

‡ Post reversal.





TABLE 5<sup>s</sup>.---Statistical Analysis of the Changes in Eight Hour Hourly Anaesthetized Postprandial Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunal Segment (E3)

Means			E1:E2				E1:E3				E2:E3				
E1*	E2†	E3‡	Confidence interval	T-value	Signifi- ficance	Confidence interval	T-value	Signifi- ficance	Confidence interval	T-value	Signifi- ficance				
Volume	1.489 1.089 3.900 5.556 6.478 6.256 5.122 4.222 34.112	2.292 2.917 5.325 12.125 10.475 7.667 7.333 4.500 52.634	6.767 6.700 10.033 13.417 10.833 6.683 10.317 9.233 73.983	- 3.295 - 4.123 - 6.003 -12.094 -10.109 - 6.528 - 9.760 - 5.066	1.690 0.468 3.153 -1.045 2.115 3.706 5.338 4.510	0.674 1.667 0.651 2.489 1.369 0.577 0.613 0.121	N.S. N.S. N.S. 5 % N.S. N.S. N.S. N.S.	-10.550 -10.216 -13.877 -15.287 -13.117 - 7.338 -16.360 -12.379	-0.005 -1.006 1.610 -0.435 4.406 6.482 5.972 2.356	2.163 2.633 1.711 3.189 1.074 0.134 1.005 1.469	5 % 5 % N.S. 1 % N.S. N.S. N.S. N.S.	- 9.573 - 8.480 -11.495 - 8.620 - 7.784 - 4.132 - 8.929 - 9.608	0.623 0.913 2.078 6.036 7.067 6.099 2.962 0.141	1.861 1.708 1.471 0.374 0.102 0.408 1.064 2.058	N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S.
Total															
Free Acid	0.068 0.084 0.449 0.600 0.797 0.804 0.672 0.462 3.936	0.226 0.300 0.567 1.634 1.437 1.033 0.947 0.557 6.701	0.955 0.058 1.458 1.745 1.513 0.903 1.297 1.107 9.936	- 0.458 - 0.518 - 0.773 - 2.026 - 1.560 - 1.028 - 1.439 - 0.812	0.142 0.086 0.537 -0.041 0.278 0.571 0.889 0.622	1.105 1.497 0.377 2.979 1.460 0.599 0.495 0.277	N.S. N.S. N.S. 1 % N.S. N.S. N.S. N.S.	- 1.642 - 1.579 - 2.228 - 2.105 - 2.088 - 1.212 - 2.357 - 1.771	-0.133 -0.168 0.209 -0.185 0.654 1.014 1.108 0.482	2.540 2.676 1.790 2.575 1.129 0.192 0.779 1.236	5 % 5 % N.S. 5 % N.S. N.S. N.S. N.S.	- 1.451 - 1.348 - 1.939 - 1.165 - 1.208 - 0.655 - 1.221 - 1.256	-0.007 0.032 0.156 0.942 1.057 0.915 0.523 0.157	2.140 2.022 1.804 0.224 0.142 0.351 0.849 1.649	5 % N.S. N.S. N.S. N.S. N.S. N.S. N.S.
Total															
Total Acid	0.074 0.088 0.462 0.624 0.823 0.830 0.689 0.539 4.129	0.170 0.308 0.510 1.565 1.585 1.066 1.098 0.658 6.960	0.985 0.982 1.487 1.805 1.573 0.928 1.127 1.138 10.025	- 0.338 - 0.547 - 0.742 - 1.837 - 1.775 - 1.113 - 1.696 - 1.010	0.146 0.107 0.647 -0.045 0.251 0.641 0.877 0.771	0.835 1.418 0.145 2.216 1.587 0.568 0.671 0.283	N.S. N.S. N.S. 5 % N.S. N.S. N.S. N.S.	- 1.680 - 1.612 - 2.261 - 2.152 - 2.150 - 1.217 - 2.219 - 1.861	-0.141 -0.176 0.212 -0.211 0.650 1.020 1.344 0.662	2.557 2.689 1.790 2.630 1.158 0.190 0.531 1.027	5 % 5 % N.S. 5 % N.S. N.S. N.S. N.S.	- 1.579 - 1.449 - 2.127 - 1.511 - 1.257 - 0.716 - 1.017 - 1.255	0.050 0.101 0.173 1.031 1.281 0.991 0.961 0.295	2.286 1.864 1.822 0.405 0.020 0.346 0.061 1.328	5 % N.S. N.S. N.S. N.S. N.S. N.S. N.S.
Total															

■ Control.

† Postenterectomy.

‡ Post reversal.



TABLE 6<sup>S</sup>.--Statistical Analysis of the Changes in Eight Hour, E, Anaesthetized Fasting Heidenhain Pouch Secretory Volumes, Free and Total Acid Concentrations, in Control Dogs (E1), Enterectomized Dogs (E2) and Dogs with an Antiperistaltic Jejunum Segment (E3)

	Mean			E1:E2			E1:E3			E2:E3					
	E1*	E2†	E3‡	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance	Confidence interval	T-value	Significance			
Volume	1.037 0.975 1.162 2.125 3.325 2.887 2.200 2.950 16.711	2.117 4.054 4.775 3.300 5.767 3.358 2.067 3.108 28.546	2.117 4.054 4.775 3.300 5.767 3.358 2.067 3.108 28.546	-3.391 -6.113 -7.140 -3.779 -7.208 -2.219 -1.426 -2.381	1.333 -0.046 -0.085 1.429 2.324 1.277 1.692 2.064	0.915 2.133 2.152 0.940 1.076 0.566 0.180 0.150	N.S. 5 % 5 % N.S. N.S. N.S. N.S. N.S.	-3.391 -6.113 -7.140 -3.779 -7.208 -2.219 -1.426 -2.381	1.333 -0.046 -0.085 1.429 2.324 1.277 1.692 2.064	0.915 2.133 2.152 0.948 1.076 0.566 0.180 0.150	N.S. 5 % 5 % N.S. N.S. N.S. N.S. N.S.	-4.598 -2.037 -5.004 -8.563 -6.121 -2.964 -4.581 -4.317	3.064 5.512 6.121 4.096 7.587 3.748 0.581 2.333	0.424 0.976 0.213 0.748 0.227 0.247 1.643 0.632	N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S.
Total															
Free Acid	0.039 0.021 0.037 0.129 0.191 0.089 0.074 0.089 0.669	0.223 0.487 0.532 0.359 0.387 0.224 0.282 0.235 2.729	0.223 0.487 0.532 0.359 0.387 0.224 0.282 0.235 2.729	-0.487 -0.884 -0.991 -0.600 -0.619 -0.301 -0.575 -0.345	0.118 -0.048 0.003 0.141 0.228 0.031 0.159 0.051	1.279 2.345 2.090 1.301 0.969 1.712 1.190 1.555	N.S. 5 % N.S. N.S. N.S. N.S. N.S. N.S.	-0.487 -0.884 -0.991 -0.600 -0.619 -0.301 -0.575 -0.345	0.118 -0.048 0.003 0.141 0.228 0.031 0.159 0.051	1.279 2.345 2.090 1.301 0.969 1.712 1.190 1.555	N.S. 5 % N.S. N.S. N.S. N.S. N.S. N.S.	-0.761 -0.291 -0.858 -1.424 -1.213 -0.576 -0.598 -0.567	0.367 0.773 0.808 0.625 0.636 0.374 0.432 0.308	0.740 0.959 0.064 0.827 0.662 0.452 0.343 0.627	N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S.
Total															
Total Acid	0.043 0.023 0.040 0.137 0.221 0.117 0.097 0.120 0.798	0.233 0.507 0.559 0.374 0.539 0.246 0.167 0.252 2.877	0.233 0.507 0.559 0.374 0.539 0.246 0.167 0.252 2.877	-0.500 -0.912 -1.026 -0.613 -0.838 -0.302 -0.226 0.342	0.121 -0.055 -0.013 0.140 0.203 0.044 0.036 0.078	1.284 2.373 2.154 1.318 1.283 1.563 0.941 1.323	N.S. 5 % 5 % N.S. N.S. N.S. N.S. N.S.	-0.500 -0.912 -1.026 -0.613 -0.838 -0.302 -0.226 0.342	0.121 -0.055 -0.013 0.140 0.203 0.044 0.036 0.078	1.284 2.373 2.154 1.318 1.283 1.563 0.941 1.323	N.S. 5 % 5 % N.S. N.S. N.S. N.S. N.S.	-0.781 -0.303 -0.883 -1.447 -1.148 -0.581 -0.565 -0.593	0.376 0.790 0.834 0.631 0.833 0.391 0.126 0.318	0.742 0.945 0.060 0.832 0.337 0.415 1.345 0.641	N.S. N.S. N.S. N.S. N.S. N.S. N.S. N.S.
Total															

\* Control.

† Postenterectomy.

‡ Post reversal



## DISCUSSION

In 1955, Hammer found 100% mortality in dogs in whom he had resected 80% of the small intestine (1). They were all dead from cachexia within ninety days of the enterectomy. The dogs in the present study all had a 90% enterectomy, and were pursuing the same downhill course as Hammer's dogs. At forty-nine days postenterectomy, or approximately one-half the anticipated survival time, an 8 cm. segment of their jejunum was reversed, to work in an antiperistaltic way. Ninety days after this, the dogs were alive and well, and their body weights stable. Although the therapeutic application of this experiment is clear, one of the unwanted side effects of the operation was an increase in gastric secretion up to 372% of the control value. This hypersecretion, the alimentary transit times, and the changes in body weight are discussed below.

### I. Increase in Gastric Secretion

The Heidenhain Pouch hypersecretion following massive enterectomy was expected, and the possible mechanisms discussed in Part I of this thesis. The further increase of Heidenhain Pouch secretion, both in volume and acid concentration, after insertion of the antiperistaltic segment, reached statistically significant levels (up to three and one-half times the controls) both in the postprandial ( $p = 0.01$ ) and the fasting ( $p = 0.05$ ) twenty-four hour collections. In a patient with a





reversed segment, acid levels of three and one-half times normal might lead to iatrogenic acid peptic disease, and, depending on the proximity of the suture line to the parietal cells, stomal ulceration.

In the eight hours awake collections, the absence of any change in Heidenhain Pouch secretion following either enterectomy or reversal suggests that random external stimuli which may act to inhibit gastric secretion are abrogated during periods of sleep or anaesthesia. The same dogs, anaesthetized, showed postenterectomy and postreversal changes over the controls of 214% and 267% (postprandial), and 156% and 172% (fasting) respectively, in Heidenhain Pouch secretion, though none of these changes was statistically significant.

The proposed causes of this gastric hypersecretion following the enterectomy are discussed in Part I of this thesis. The suggested cause of gastric hypersecretion following reversal in antral stasis. Delayed gastric emptying was produced by inserting the antiperistaltic segment close to the pylorus, just beyond the distal end of the duodenum, and in several of the barium studies, reflux through the pylorus was demonstrated. Pictorial proof of prolonged stimulation of the antrum demonstrates a possible explanation of the elevated Heidenhain Pouch secretion after segmental reversal.

## II. Increase in Transit Time

In the normal gastrointestinal tract, the ileo-cecal valve acts as a control, causing a delay in transit of the luminal content. Experiments in which the ileo-cecal valve has been bypassed have shown a subsequent intestinal hurry, with absorptive losses (2). In a shortened





intestine, the insertion of an antiperistaltic segment serves the same function, namely to increase the length of time that the foodstuffs are in contact with the intestinal absorbing surface, and so produce an increased uptake of nutrients. There is a fine line between a segment long enough to affect transit time significantly, and yet short enough not to produce a pathological obstruction. The optimum length varies according to the site of insertion, generally increasing in length as the site becomes more distal, and the absorptive power less (3, 4, 5). The aim of the procedure is to promote maximum absorption of nutrients from the intestinal tract by prolonging alimentary transit time.

In our study, the mean gastric emptying time was increased from four and one-half to six hours. The delay is demonstrable only proximal to the site of the antiperistaltic segment; and when this treatment is used therapeutically, the position of insertion will be determined by the clinical condition. For example, Poth has constructed pouches containing iso- and antiperistaltic components to replace the stomach (6) in the treatment of the dumping syndrome, while other surgeons have, with some benefit, reversed a segment between stomach and duodenum, or immediately distal to the Ligament of Treitz. Postvagotomy diarrhea has also responded to this treatment in the hands of some workers (8). Should the therapy be to compensate for massive loss of small intestine, as in the treatment of mesenteric thrombosis, volvulus, Crohn's disease, extensive cancer or trauma, the segment may be placed in such a position as to maintain the luminal content in the area where absorption is thought to be greatest, for the longest possible time. Investigators have suggested a point about 90 cm. below the Ligament of Treitz as the site of



election in man (9). In addition to the weight loss, diarrhea, steatorrhea, hypoproteinemia, and hypocalcemia that follows massive enterectomy, the severe losses of Vitamins B<sub>12</sub> and C have proved troublesome; and absorption of these elements is usually complete by the first 100 cm. distal to the Ligament of Treitz. Other investigators have noted that in mesenteric artery thromboses, only about 30-40 cm. of jejunum survives distal to the Ligament of Treitz, as a result of the collateral blood supply from the pancreaticoduodenal artery (7). For this reason, their experimental work has used reversed segments at about 40 cm. distal to the Legament of Treitz, with favorable results, namely the preservation of nutrition and body weight.

### III. Decline in Body Weight

Immediately after enterectomy, the dogs began to lose weight at a mean rate of 1 kg. a week, for two weeks, and then more gradually at 1 kg. every two weeks, for the next six weeks. The rapid early weight loss probably represents the additive effects of surgical stress, intravenous feeding for several days, and the grossly shortened intestinal absorbing surface, while the more gradual later losses indicate the purely anenteric element. In support of this conclusion, it was found that by the end of two weeks after insertion of the anti-peristaltic segment, the effects of the operation were apparent: four of the dogs had begun to gain weight slowly, and the steep fall (in the two smallest dogs) had been arrested. The mean weights then levelled off.



The immediate cause of weight loss in the short bowel syndrome is probably failure of fat absorption. Although all three main food constituents are less effectively absorbed after enterectomy, investigators have shown that fat absorption is more impaired than that of protein or carbohydrate (10, 11). The resultant steatorrhea and weight loss has been partially compensated by the oral administration of medium chain triglycerides (12). Methscopolamine bromide (epoxytropine tropate methylbromide<sup>\*</sup>) 2.5 mg. per kg. body weight twice a day has been added by Hammer and his associates to the diet of 80% enterectomized dogs, with survival, against similarly enterectomized dogs who received no methscopolamine, which all died. Two of the six dogs receiving methscopolamine were then taken off it, and also died, while their colleagues still receiving the drug all lived (13).

At the conclusion of our study, the mean body weight of our dogs was steady at 75% of their control weight, and the dogs were healthy. Autopsy showed the reversed segments to be uncomplicated, and the intestine proximal to the segments to be dilated. Some workers have reported a narrowing both in length and breadth of the reversed segment in long term follow-up, although its therapeutic function remained unimpaired, and biopsy was normal (13, 14). Trichobezoar formation in dogs has resulted in fatal obstruction when the reversed segment is placed near the ileo-cecal valve, possibly exacerbated by the narrowing of the segment with time (15). A rare complication in this regard has been the formation of bezoars from splinters and wood shavings chewed off wooden

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\* "Pamine".





cages by the dogs postoperatively; and a clinical precaution after this procedure on patients would be to restrict the intake of high residue foodstuffs, such as oranges, capable of producing a low obstruction.



## FOOTNOTES

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